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# Assessment of listing and categorisation of animal diseases within the framework of the Animal Health Law (Regulation (EU) No 2016/429): bluetongue

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## Abstract

A specific concept of strain was developed in order to classify the BTV serotypes ever reported in Europe based on their properties of animal health impact: the genotype, morbidity, mortality, speed of spread, period and geographical area of occurrence were considered as classification parameters. According to this methodology the strain groups identified were (i) the BTV strains belonging to serotypes BTV-1–24, (ii) some strains of serotypes BTV-16 and (iii) small ruminant-adapted strains belonging to serotypes BTV-25, -27, -30. Those strain groups were assessed according to the criteria of the Animal Health Law (AHL), in particular criteria of Article 7, Article 5 on the eligibility of bluetongue to be listed, Article 9 for the categorisation according to disease prevention and control rules as in Annex IV and Article 8 on the list of animal species related to bluetongue. The assessment has been performed following a methodology composed of information collection, expert judgement at individual and collective level. The output is composed of the categorical answer, and for the questions where no consensus was reached, the different supporting views are reported. The strain group BTV (1–24) can be considered eligible to be listed for Union intervention as laid down in Article 5(3) of the AHL, while the strain group BTV-25–30 and BTV-16 cannot. The strain group BTV-1–24 meets the criteria as in Sections 2 and 5 of Annex IV of the AHL, for the application of the disease prevention and control rules referred to in points (b) and (e) of Article 9(1) of the AHL. The animal species that can be considered to be listed for BTV-1–24 according to Article 8(3) are several species of Bovidae, Cervidae and Camelidae as susceptible species; domestic cattle, sheep and red deer as reservoir hosts, midges insect of genus *Culicoides* spp. as vector species.



**Keywords:** bluetongue, strain, serotypes, impact, Animal Health Law, Listing, categorisation

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## Summary

The European Commission has requested the European Food Safety Authority (EFSA) to provide an updated scientific advice on bluetongue (BT), due to the recent disease evolution in the European Union (EU), the experience gained from the BT control policies and possible alternative methods to ensure safe trade of live animals from BT restricted zones. The scientific advice asked from EFSA should serve to review the overall BT policy at the EU level. The terms of reference of this request covered different topic areas, in particular related to (1) BT control policy through vaccination and surveillance; safe trade of animals moved from BT virus (BTV) infected to BTV-free country or zone, both (2) about animal immunity and (3) protection from BTV vectors; (4) classification of BT serotypes and (5) BT listing and categorisation in the framework of the Animal Health law (AHL). The first three categories were covered in a previous opinion, the present one covers the fourth and fifth topic area.

As regards the topic about classification of BT serotypes, it was requested to review and provide an update of existing serotypes in the EU and elsewhere. This was done by describing, based on the relevant literature, the existing BT serotypes that have been or are present in Europe and in neighbouring countries in chronological order and in relation to the country or area of occurrence.

Secondly, it was requested to assess, by using appropriate criteria, the feasibility of grouping the currently known BTV serotypes in appropriately defined groups of serotypes sharing similar properties concerning the impact on animal health. If the serotype classification is useful for the production of serotype-specific vaccines, the classification based on serotypes to assess the different level of impact is not sufficient to fully represent the genomic diversity and pathogenic heterogeneity of BTV. In the past, in fact, different virus strains belonging to the same serotypes have caused very different pictures in terms of animal health impact in Europe and elsewhere. Rather, for this purpose, a specific concept of 'strain' has been developed: this includes the classification according to serotype, genetic diversity (genotype) together with other aspects of epidemiological relevance, morbidity, mortality, case-fatality rates, host spectrum, the speed of spread, the period and the geographical area of occurrence, and their ability to actively circulate within different episystems, as calculated from Animal Disease Notification System (ADNS) data. These epidemiological parameters were expressed quantitatively for both cattle and small ruminants, and they were ranked and combined to calculate a pathogenicity score in order to estimate a measure of the impact on cattle and small ruminants. According to this methodology, the proposed grouping based on BTV strains as defined in the present opinion is:

- BTV strains belonging to serotypes BTV-1, -2, -4, -8, -9 that have circulated or are still circulating in some parts of Europe.
- Some strains of serotypes BTV-16 still circulating in some parts of Europe.
- Small ruminant-adapted strains (BTV strains belonging to serotypes BTV-25, -27, -30 and related isolates).

According to the outcome of the assessment mentioned above, it was requested to assess whether any of the above serotypes/groups of serotype could be candidates for a partial or total exclusion from the overall BT policy currently in place in the EU, linked to their low level of virulence or pathogenicity. According to the assessment here presented, the only BTV serotypes that could be partially excluded from the overall BT policy currently in place in the EU, due to their low level of virulence or pathogenicity, are the small ruminant-adapted strains (serotypes BTV-25, -27, -30). Nevertheless, surveillance is needed both within the EU and in neighbouring areas that can be a source of future incursions both to provide a better understanding/prediction of the likelihood of an incursion into Europe, as well as to detect new BT outbreaks within Europe, to identify both their significance (severity, rate of spread, serotype, genotype and host species involvement) and to develop appropriate control strategies. For this purpose, appropriate surveillance strategies/methods, including sentinels and the importance of passive surveillance, should be refined and publicised, as well as a well-established and identified surveillance network to detect outbreaks at an early stage, in order to characterise the virus in cause and to assess their relative economic importance and their impact on animal health. If new outbreaks can be identified early on, an appropriate 'ring vaccination' strategy could be developed to reduce/prevent viral spread and the potential for further outbreaks. If a broader cross-reactive (cross-serotype) BTV vaccine, ideally with DIVA capability and long shelf-life, could be developed, this would potentially reduce the number of different vaccine preparations required and therefore potentially reduce the costs of a vaccine bank.

The strain groups identified above, are further considered for the assessment of Term of Reference (ToR) 5, i.e. the assessment on listing and categorisation of BT in the framework of the AHL, in particular about the criteria of Article 7 on disease profile and impacts, Article 5 on the eligibility of BT strain groups to be listed, Article 9 for the categorisation of BT strain groups according to disease prevention and control rules as in Annex IV and Article 8 on the list of animal species related to BT.

The assessment has been performed following a methodology composed of information collection and compilation, expert judgement on each criterion at individual and, if no consensus was reached before, also at collective level. The output is composed of the categorical answer, and for the questions where no consensus was reached, the different supporting views are reported. Details on the methodology used for this assessment are explained in a separate opinion.

According to the assessment here performed, the strain group BTV (1–24) can be considered eligible to be listed for Union intervention as laid down in Article 5(3) of the AHL, while the strain group BTV-25–30 and BTV-16 do not comply with criterion A(iii) of Article 5 and therefore cannot be considered eligible to be listed for Union intervention as laid down in Article 5(3) of the AHL.

According to the assessment here performed, the strain group BTV (1–24) meets the criteria as in Sections 2 and 5 of Annex IV of the AHL, for the application of the disease prevention and control rules referred to in points (b) and (e) of Article 9(1) of the AHL. Since BTV-25–30 and BTV-16 cannot be considered eligible to be listed for Union intervention as laid down in Article 5(3) of the AHL, the assessment of its compliance with each of the criteria in Annex IV to the AHL for the purpose of categorisation of diseases in accordance with Article 9 of the AHL is not applicable.

According to the assessment performed here, the animal species that can be considered for listing for BTV-1–24 according to Article 8(3) of the AHL are several (potentially all) species of Arctiodactyla belonging to the families of Bovidae, Cervidae and Camelidae as susceptible species; domestic cattle, sheep and red deer as reservoir hosts; midges insect of genus *Culicoides* spp. as vector species for BTV-1–24.

Since BTV-25–30 and BTV-16 cannot be considered eligible for listing for Union intervention as laid down in Article 5(3) of the AHL, the assessment of the animal species that are considered to be listed in accordance with Article 8 of the AHL is not applicable.

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# 1. Introduction

## 1.1. Background and Terms of Reference as provided by the European Commission

Over the past 20 years, bluetongue (BT) incursions of a variety of serotypes occurred and on several occasions became widespread across many parts of Europe. Affected countries sometimes adopted diverse control policies, particularly as regards vaccination against the disease in order to cope with both the short as well as the long-term consequences in animal health, animal production and trade of live animals or their products. Incidences of BT during this period have included unexpected epidemics in areas, where it had not appeared for more than 10 years (e.g. blue tongue virus 4 (BTV-4) in the mainland of the Balkan Peninsula in 2014), but also low-impact circulation of certain serotypes (some of them of unclear origin), incursions of new serotypes, vaccine incidents and disease resurgence (BTV-8 in France in 2015), raising concerns and evidencing new challenges.

The European Commission has repeatedly sought scientific advice on BT from the European Foods Safety Authority (EFSA) in the last decade and in response, EFSA has produced a number of scientific opinions dealing with various aspects of BT epidemiology, surveillance and control, which provided valuable conclusions and recommendations that have helped to shape the current disease strategy at the European Union (EU) level. Nevertheless, an update appears necessary in the light of the recent disease evolution, the current epidemiological situation, the experience gained so far from the implementation of the various BT control policies and possible alternative methods to ensure safe trade of live animals from BT-restricted zones and the latest scientific information available. The need to review the overall BT policy at EU level is an issue that has been repeatedly emphasised by national authorities of many Member States (MSs), and the IV International Conference on Bluetongue and related orbiviruses (Rome, 5–7 November 2014) represents a major milestone for taking stock of the latest state of the art science on BT.

In order to streamline the way forward, the Commission with the MSs have identified a series of issues for which concrete elements of science may provide a good basis for reformulating policies and/or adapting current rules. These are as follows:

1) Safe trade provisions

As regards provisions for safe trade, in particular from BT-restricted areas, the European Commission, on top of those already in place in Commission Regulation (EC) 1266/2007, is keen to explore other options used by the competent authorities of some EU Member Countries in the framework of bilateral trade agreements drafted in accordance with Article 8 of the same Regulation. Article 8 of Commission Regulation (EC) No 1266/2007 foresees that exemptions from the exit ban are to be based on risk mitigating measures presented in Annex III to the Regulation or on any other appropriate animal health guarantees based on a positive outcome of a risk assessment agreed between the competent authority of the place of origin and the competent authority of the place of destination. Currently, there are such agreements on the movement of live animals concluded between France and Italy of 2015, France and Spain of 2013 and 2015, Italy and Spain of 2012, Spain and Portugal of 2014, France and Luxembourg of 2015 and Italy and Austria of 2016.

2) Classification of different BTV serotypes

There are indications that more than 27 different serotypes of the BTV have been identified to date. Each of these serotypes, apart from its specific genetic and antigenic features, may also be connected with specific epidemiological and pathogenicity properties. It is necessary to understand whether it is possible to use these properties as a set of standard criteria to divide known BT serotypes in groups, each deserving a distinct treatment as regards surveillance, protection and control measures.

3) BT listing and categorisation in the framework of the AHL

In addition to the classification of the different serotypes, BT merits an assessment as part of the listing and categorisation exercise of animal diseases in the framework of the Animal Health Law (AHL) in the same manner as it was requested previously for another seven diseases (Ref. SANTE G2/BL/lp (2015) 4940871).

In the light of the above-mentioned ongoing procedure, the Commission is in need of scientific advice on the assessment of the significance of BT (as an integral disease, or separately for each serotype or group of serotypes, depending on the outcome of the grouping exercise) also within the

framework of the listing and categorisation according to the AHL. The criteria, provided for ease of reference in Annex II and Attachments I to IV thereof, shall be used as a basis for this analytical assessment. The risk manager needs an updated scientific advice in order to:

1) assess if the various serotypes or groups of serotypes of BTV cause diseases for which control measures at the EU level are justified;
2) proceed with the profiling of the diseases caused by the serotypes or groups of serotypes of BTV as above in view to their categorisation; and
3) assign listed species to the various serotypes or groups of serotypes of BTV identified as eligible for EU intervention.

### 1.1.1. Terms of Reference

In view of the above, and in accordance with Article 29 of Regulation (EC) No 178/2002, the Commission asks EFSA for a scientific opinion under the following headings:

**1. As regards vaccination, eradication and surveillance**

1.1 Assess the most suitable duration of a BT vaccination campaign intended to achieve disease freedom in a country or region considering any relevant factors that may affect and influence disease spread, and persistence.

1.2 Assess the probability of BT recurrence in BT-affected areas that have regained BT freedom, in particular due to BT virus becoming endemic with low level circulation in these areas and reoccurring 'spontaneously' (low-noise circulation in livestock or wildlife, maintenance in vectors or other possible mechanism to be considered).

1.3 Revise and assess the suitability of the provisions on surveillance laid down in Regulation (EC) No 1266/2007 to ensure reliable and robust demonstration of absence of virus transmission in a MS or epidemiologically relevant area, considering point 1.2 above.

**2. As regards specific options for safe trade that could be used for exemptions from the exit ban applicable to movements of live animals from a restricted zone**

2.1 Assess whether maternal immunity against BT in calves, lambs and kids born to, and colostrum fed from, vaccinated mothers, constitutes a sufficient guarantee for animals of the above species to be moved safely from a BTV-infected to a BTV-free country or zone, without a risk for disease spread, with or without the need for any additional premovement testing regime and indicate the main parameters that could be used (minimum/maximum age of calves, testing of dams, etc.).

2.2 Assess the minimum age of calves, lambs and kids after which residual colostral antibodies against BTV do not interfere any longer with vaccine immunisation of these animals (in an example of BT bilateral agreement this age limit is set at 90 days).

2.3 Assess the minimum time after completion of the primary vaccination (1–2 doses as indicated by the vaccine manufacturer) for the vaccinated animals to be considered immune to be safely moved from a BT-infected to a BT-free country or zone (currently set at 60 days in paragraph 5 of Annex III to Regulation (EC) No 1266/2007).

2.4 Assess whether vector protection for 14 days of ruminants below the age of 70 days, combined with a negative polymerase chain reaction (PCR) test at the end of the 14 days or more, qualify them for a safe movement from a BT-restricted to a BT-free area.

**3. As regards protection from BTV vectors and vector-based provisions for exemption from the exit ban applicable to movements of live animals from a restricted zone**

3.1 Review and update previous opinions as regards vectors ecology (models for distribution/density), in order to have more accurate and applicable criteria for the determination of the seasonally vector-free period.

3.2 Review and update previous opinions as regards over-wintering mechanisms and the duration of the BT viraemia.

3.3 Review and update previous opinions and provide a scientific assessment of the appropriateness of the use of insecticides and repellents against *Culicoides* as BT competent vectors, including an assessment of their efficacy and recommendations of adequate protocols for their uses, in particular as regards their suitability to protect animals against attacks by vectors performing at least equal to the protection provided by vector-proof establishments – without the need to keep animals in a vector protected facility.

**4. As regards classification and grouping of different BTV serotypes according to their potential impact on animal health**

4.1 Review and update previous opinions providing a short description of existing serotypes in the EU and elsewhere.

4.2 Assess, by using appropriate criteria, the feasibility of grouping the currently known BTV serotypes in appropriately defined groups of serotypes sharing similar properties thus creating a number of 'BTV serotype groups' separated by significant different levels of impact on animal health (e.g. most serious clinical symptoms in many individuals in large areas, mild symptoms to few individuals within small areas or no symptoms at all in one or more BT susceptible species etc.).

4.3 Review and classify the existing serotypes according to the outcome of the assessment in point 4.2 above and assess whether any of the above serotypes/groups of serotype could be candidates for a partial or total exclusion from the overall BT policy currently in place in the EU, in particular due to their low level of virulence or pathogenicity.

**5. Listing and categorisation of BT in the framework of the Animal Health Law.**

5.1 Considering the outcome of the assessments and reviews referred to in paragraph 4 above, for each of the aforementioned groups of serotypes, or BT in general as appropriate, assess, following the criteria laid down in Article 7 of the AHL, its eligibility of being listed for Union intervention as laid down in Article 5(3) of the AHL;

5.2 Considering the outcome of the assessments and reviews referred to in paragraph 4 above, for each of the aforementioned groups of serotypes, or for BT in general, if found eligible to be listed for Union intervention, provide:

a) an assessment of its compliance with each of the criteria in Annex IV to the AHL for the purpose of categorisation of diseases in accordance with Article 9 of the AHL;
b) a list of animal species that should be considered candidates for listing in accordance with Article 8 of the AHL.

## 1.2. Interpretation of the Terms of Reference

The first three Terms of Reference (ToRs) have been addressed in a previous opinion (EFSA AHAW Panel, 2017a), while the present opinion answers the ToR 4 and 5. The BTV serotypes that will be considered in this opinion are the ones that have been reported in the EU (BTV-1, BTV-2, BTV-4, BTV-8, BTV-9, BTV-16, BTV-25, BTV-26 and novel strains). Vaccine strains are not considered in this document since they are not disease-causing agents and hence are not under the scope of the mandate. Nevertheless it should be considered that:

- Live vaccine strains like BTV-11, -14, -6 (which have disappeared from the EU) and -16 (which is still circulating in the EU), may still spread in the field, and entail possible risks.
- The viruses circulating in the field can also reassort (exchange genetic material) with live vaccine virus(es), generating novel strains with unknown characteristics.
- Since live BTV vaccines are no longer used in the EU, in case of re-occurrence, these would be considered as field strains.

The assessment on ToR 4.1 reviewing existing serotypes that have been or are present in Europe and in neighbouring countries is presented in Section 3.1. The occurrence of BT epidemics for each serotype is described in chronological order and in relation to the country or area of occurrence.

The ToR 4.2 on the assessment of grouping the currently known BTV serotypes according to significant different levels of impact on animal health is discussed in Section 2.2 where the principle and the criteria for grouping BT serotypes and strains are discussed. The outcome of this is presented in Section 3.2, which addressed the ToR 4.3 about the classification of the existing serotypes and strains and assesses whether any of these could be candidates for a partial or total exclusion from the overall BT policy currently in place in the EU, due to their low level of virulence or pathogenicity.

The assessment on ToR 5 about listing and categorisation of BT in the framework of the AHL is addressed in Sections 3.3 (assessment on Article 7 criteria of AHL), 3.4, 3.5 and 3.6. The approach followed is that used for other opinions dealing with assessment of listing and categorisation according to the AHL (EFSA AHAW Panel, 2017b).

# 2. Data and methodologies

## 2.1. Data

The data used in this opinion are taken from the scientific literature on BT, from the Animal Disease Notification System (concerning epidemiological data on BT reported from MSs), and from previous EFSA opinions on bluetongue (EFSA AHAW Panel, 2017a). Data reported in the presentations given during the meetings of the Standing Committee on Plants, Animals, Food and Feed[1] are also considered.

## 2.2. Methodologies

BTV is classically subdivided in different serotypes according to the immunological and neutralisation characteristics of viral protein (VP) 2, which is the major protein involved in stimulating the production of serotype-specific neutralising antibodies in vertebrate hosts. Given the lack of effective cross-protection mechanisms between serotypes, the serotype classification is extremely useful for the identification and production of serotype-specific vaccines that are able to protect against the homologous BTV. However, the classification based on serotypes is not sufficient to fully represent the genomic diversity and pathogenic heterogeneity of BTV. Therefore, considering that, an assessment of the impact of different 'types' of BTV is requested, a specific concept of 'strain' has been developed, merging the classification according to serotype, genetic diversity (genotype) together with other aspects of epidemiological relevance, including the period and the geographical area of occurrence. In the past, in fact, different virus strains belonging to the same serotypes have caused very different pictures in terms of animal health impact in Europe and elsewhere.

For example the BTV-1 circulating in Greece in 2001 that showed genetic similarities to eastern (Indian) viruses, caused minor consequences on animal health and was associated to mild clinical signs in sheep only. In 2007, another BTV-1 of different provenance (related to African strains), however, spread from Morocco through the Iberian peninsula to France, and persisted in these territories for a number of years, causing significant animal health problems due to its capacity to produce severe disease in sheep flocks. These two BTV strains are genetically diverse, despite belonging to the same serotype.

Although the analytical work done can characterise each BTV strain, it is noteworthy to clarify that BTV infection is a dynamic process. The interaction between virus and host is a process that is under constant adaptation and evolution. Different virus lineages can interact genetically, and are continuing to evolve. The immune status and the susceptibility of the local ruminant host population may also change significantly. It may therefore be difficult to extrapolate evidence from the past for a specific BTV strain, to a future occurrence, unless with clear linkages in time and space. On the other hand, the behaviour of a certain BTV serotype or strain, including its ability to spread in a new, previously unaffected, area cannot be reliably estimated on the basis of what happened in other territories. Animal health impact is a complex combination of several factors working together in that specific circumstance and epidemiological system.

Still, the connection between genomic information with field-biological information is important: some laboratory tools can support the differentiation of biological characteristics, although at the moment it is not possible to identify clear genetic markers or biological tests for predicting virulence, severity and rate of spread of an outbreak in the field. Therefore, observations during the early stage of an outbreak are potentially the most important indicators of the threat to animal health.

The parameters considered for assessing the animal health impact were morbidity, mortality and case-fatality rates, calculated on the basis of the Animal Disease Notification System (ADNS) data in each outbreak and for each BTV strain. Moreover, in order to assess the spread capacity of the BTV strains, the mean number of outbreaks per week, as reported to ADNS, was considered, together with the ability to actively circulate within different epidemiological systems (episystems). The concept of episystem was initially proposed by Tabachnick et al. (2004) and recognises that specific BTV strains may be better adapted to, and therefore to some extent restricted to, certain geographic regions. These adaptations reflect the specificity of their interactions with the local vector and host populations, which may be influenced by climate and other factors, as demonstrated by previous BTV history and

[1] https://ec.europa.eu/food/animals/health/regulatory_committee/presentations_en

the identity of circulating strains in the region. For the purposes of the present opinion and focussing on the European continent and the Mediterranean Basin, three major episystems can be observed:

- South-western European episystem, including the western Mediterranean area and characterised by the relatively high abundance of the major BT vector, *Culicoides imicola*, large sheep populations and high probability of exposure to the introduction of BTV strains from northern African countries, frequently through infected midges disseminated by winds.
- South-eastern European episystem, covering the Balkan and the eastern Mediterranean zones, characterised by an heterogenicity of vector species involved in the BTV transmission, with the presence of *C. imicola* in limited areas of Greece and Turkey and the presence of other species belonging to the Obsoletus and Pulicaris complexes in the other zones of the area, a lower density of sheep population and the exposure of the incursions of BTV strains from Asia and Middle East.
- Northern and central European episystem, characterised by the transmission of BTV by *Culicoides* species belonging to the Obsoletus and Pulicaris complexes and other cattle-related species, such as *C. chiopterus* and *C. dewulfi*, and climatic conditions in general less favourable to *Culicoides* borne diseases.

It must be underlined that the three above reported episystems cannot be considered an exhaustive description of BTV epidemiological niches present in Europe. They have been chosen given the purposes of this study. Considering a smaller scale and geographical resolution, in fact, multiple BTV episystems could be identified, for example, in countries with highly geographic and climatic variations, like Italy (south-east and south-west).

Regarding grouping BTV strains based on levels of impact on animal health, the main criteria concerning pathogenicity, epidemiological properties and geographical spread have been considered for assessing the animal health impact of BTV strains as described in the Section 2.2.

The pathogenicity of each strain has been assessed considering the severity of clinical symptoms in the main susceptible species (domestic cattle and small ruminants), as measured by the within-herd morbidity, mortality and case fatality rates, calculated from the ADNS data. These rates are expressed quantitatively for both cattle and small ruminants as median, 5th and 95th percentiles. Based on the 95th percentile of each epidemiological parameter, a pathogenicity score is calculated in order to estimate a measure of the impact on cattle and small ruminants, as explained in the table legend (Table 2).

Data on production and reproduction losses different from direct mortality of animals (e.g. weight and/or milk loss or losses linked to fertility reduction) is limited and available only for BTV-8, and therefore these aspects have not been taken into account in this analysis (Rushton and Lyons, 2015).

Moreover, as a measure of speed of spread, the mean number of outbreaks per week reported to ADNS (in the period where no vaccination was implemented) has been calculated and categorised in three classes (low, medium and high) according to $< 50$ outbreaks/week, between 50 and 150 outbreaks/week, and $> 150$ outbreaks/week.

Some further aspects related to epidemiological properties have been considered: the transmission routes (vector-borne or direct), the capability of spread in different episystems and the host spectrum.

For the purposes of what requested by ToR 4, the above reported criteria have been used to categorise the main BTV strains on the basis of the animal health impact.

Considering the impossibility of categorising a priori BTV strains from their pathogenicity capacity point of view, an empirical approach was followed in the present opinion, by analysing the observed and notified data on BTV outbreaks in the EU. This approach can be affected by some biases, not only due to the underreporting phenomenon, but also because what observed in the different circumstances was strictly related to the specific and local epidemiological conditions, such as abundance and distribution of competent vectors, density of susceptible animal hosts, period of the year of BTV introduction into the susceptible population. This approach, therefore, cannot be able to predict the impact the infection due to the same serotype in different epidemiological conditions and the conclusions that can be driven from the current assessment are limited to what already observed in the past in the EU.

Regarding ToR 5, the methodology applied in this opinion is described in detail in a dedicated document about the ad hoc method developed for assessing any animal disease for the listing and categorisation of diseases within the AHL framework (EFSA AHAW Panel, 2017b).

It is noteworthy to highlight that although the impact on different animal species has been not considered separately in the assessment according to article 5 and 9 criteria, BTV infection results in a

clearly distinct clinical picture between sheep and cattle. In the latter, in fact, with the sole exception of BTV-8 epidemic in France, Belgium, Germany and the Netherlands in 2006–2008, clinical cases are usually rare and the mortality absent.

# 3. Assessment

## 3.1. Review of existing BTV serotypes

This section described the main serotypes that have occurred in Europe and in the Mediterranean basin and neighbouring countries. Historically (prior 1998), Europe had experienced only sporadic incursions of BT, involving a single virus serotype on each occasion (Mellor and Boorman, 1995).

A major outbreak caused by BTV-10 ravaged the sheep populations of Spain and Portugal between 1956 and 1960, causing the deaths of almost 180,000 animals (Manso-Ribeiro et al., 1957) and a smaller outbreak of BTV-4 occurred on several Greek islands near the Anatolian Turkish coast in 1979 (Vassalos, 1980). However, since 1998, BTV has spread northwards into the Mediterranean Basin, with new strains of five BTV serotypes (1, 2, 4, 9 and 16) have been identified in each successive years (Purse et al., 2005). BTV-9 first entered eastern Europe (Greece) in 1998. Between 1999 and 2002, this strain spread from Greece to Bulgaria invading all of the Balkan Peninsula and southern mainland Italy (November 2000–2001).

In Greece, BTV-16, BTV-4 and BTV-1 strains were also isolated in 1999, 2000 and 2001, respectively (Panagiotatos, 2004). In 2000, BTV-2 was confirmed for the first time ever in Italy. The island of Sardinia was affected first but by October, BTV-2 had also spread to Sicily and southern mainland Italy. BTV-2 was also recorded for the first time on the French island of Corsica, and on the Spanish islands of Menorca and Mallorca. Just as in Italy, the outbreaks in the Balearics continued into November and December 2002 (Mellor, 2004).

In 2002, BTV-16 was also reported from southern Italy (Puglia). BTV-16 seroconverted sentinel animals were found in October 2003 (OIE, 2004a) in Cyprus. In February 2004, a new outbreak of BT occurred in Larnaca district, also in the eastern part of the country. In January 2004, circulation of BTV-16 in Sardinia was detected by virus neutralisation test in seven sentinel animals (Calistri et al., 2004a). In the summer of the same year, BTV-16 (vaccine strain) was detected also in Corsica (OIE, 2004b).

In September 2003, circulation of BTV-4 was detected in Sardinia (OIE, 2003a), in October BTV-4 was identified at the laboratory of the French Agency for Food Safety (AFSSA) (OIE, 2003b). In the same year, BTV-4 was also identified from the Spanish Balearic islands.

A vast epidemic of BTV-4 in 2004 involved also the northern part of Morocco (OIE, 2004c), spreading from there into the southern part of the Iberian Peninsula (OIE, 2004d,e).

The phylogenetic analyses of BTV detected in the Spanish island of Menorca showed that this was also a western strain of BTV-4, although it was clearly distinct from strains that had previously caused outbreaks in the eastern Mediterranean region.[2] These conclusions were confirmed by Zientara et al. (2006) working with Corsican isolates. This virus was believed to have entered Europe from North Africa. The same strain of BTV-4 subsequently caused outbreaks and was isolated in Morocco and then spread to the Iberian Peninsula in 2004, where it persisted through into 2005.

In 2006 (October), BTV-1 was recorded in Sardinia (OIE, 2006). This serotype subsequently spread from Maghreb to southern Spain, where it was detected in the summer of 2007 (OIE, 2007c). BTV-1 continued to spread during 2007 and was detected in Portugal by September (OIE, 2007a) and south-west France in November (OIE, 2007b). By November 2008, BTV-1 had spread as far as Brittany in northern France (ISID, 2008).

In the summer of 2006, for the first time, BTV crossed latitude 50°N and outbreaks caused by BTV-8 occurred in north-western Europe: the Netherlands, Belgium, Germany, France, and Luxembourg (Wilson and Mellor, 2008). In 2007–2008, the BT situation changed for the worse, BTV-8 spread to the other regions of Europe and the number of outbreaks increased rapidly. Additionally, two new BTV serotypes, BTV-11 and BTV-6 (both South African vaccine strains) were detected (Wilson and Mellor, 2009). However, the implementation of BT vaccination programmes in Europe resulted in a massive reduction of BTV-8 cases, and even eradication in some countries.

In 2012, BTV-1 and BTV-4 were identified in Sardinia and BTV-14 (vaccine strain) in Lithuania, Latvia, Poland and Spain. In 2013, disease caused by BTV-1 spread extensively over the territory of

[2] www.iah.bbsrc.ac.uk/dsRNA_virus_proteins/ReoID/btv-4.htm; http://www.iah.bbsrc.ac.uk/dsRNA_virus-proteins/ReoID/BTV-mol-epidem.htm

Italy (Sardinia, Sicily and mainland Italy). At the beginning of 2014, the same BTV serotype was isolated in Corsica (France). Moreover, in 2013, BTV-1 cases were noticed in western Spain, while outbreaks caused by BTV-4 were observed in southern Spain (Andalusia) and in the region of the Algarve in Portugal. In 2014, more cases associated to BTV-4 and BTV-1 were recorded in Spain. In 2014, outbreaks of BTV-4 were confirmed in Greece (Peloponnese and Evros regions). In July, the first outbreak of BTV-4 was also reported in the south of Bulgaria and from there it spread to the rest of Bulgaria, Romania and all of the Balkan countries and southern Italy. In 2015, BTV-4 spread to Austria and Slovenia and continued circulating in the Balkan Peninsula and Italy, where in 2016 the strain affected nearly all of the country including the northern regions and part of Sardinia.

In 2015, despite 5 years of supposed absence, BTV-8 re-emerged in France and in 2016 spread further, affecting almost all the country. In 2015 and 2016, few BTV-1 and BTV-4 outbreaks were recorded in Spain, whereas BTV-1 circulation was still observed in Portugal.

A new BTV strain infecting goats was discovered in Switzerland in early 2008. It was initially named Toggenburg orbivirus (Hofmann et al., 2008; Chaignat et al., 2009). This strain has been confirmed as a novel serotype, BTV-25.

In February 2010, another novel BTV serotype was isolated in Kuwait from sheep and named BTV-26 (virus isolate KUW2010/02) (Maan et al., 2011a). When experimentally infected with BTV-26, sheep showed only mild clinical disease (Batten et al., 2012). Phylogenetic analyses showed a high level of divergence in most of the conserved genome-segments between most BTV strains and BTV-26 (KUW2010/02) and/or BTV-25 (SWI/2008/01), placing them as representatives of two novel and distinct BTV topotypes (Maan et al., 2011b). The kinetics of BTV-26 infection in sheep and goats are similar to those of BTV-25. Although this virus replicates well in mammalian cells, it does not infect cells or adults of a vector (Pullinger et al., 2016). However, the virus can be horizontally transmitted to uninfected, in-contact goats, which subsequently seroconvert (Batten et al., 2013a, 2014). This indicated that unlike BTV-25, BTV-26 can be transmitted horizontally by direct contact and replicates in mammalian cells (BHK-21, BSR and Vero cells) *in vitro*, but does not replicate in KC cells. There is serological evidence that the distribution of BTV-26 may be more widespread, in cattle and camels in Mauritania (Lorusso et al., 2016).

During the compulsory vaccination programme against BTV-1 in Corsica (France) in 2014, a BTV strain belonging to a previously uncharacterised serotype (BTV-27) was isolated from asymptomatic goats (Zientara et al., 2014). Three variants of BTV-27 have been described (Schulz et al., 2016). The full coding genome of the two novel BTV-27 variants (isolated in 2015 in Corsica) show high homology (90–93 % nucleotide/93–95 % amino acid) with the originally described BTV-27 isolate from Corsican goats in 2014. These three variants constitute the novel serotype BTV-27 ('BTV-27/FRA2014/v01 to v03').

During Bluetongue surveillance activities, Savini et al. (2017) identified a putative novel BTV serotype in healthy goats from Sardinia, Italy. Overall, Seg 2 of BTV-X ITL2015 shows the highest identity with recently isolated BTV-27s from Corsica and with the last discovered BTV XJ1407 from China, whereas it is less related with BTV-25 from Switzerland and BTV-26 from Kuwait. Considering the Seg 2/VP2 identity of BTV-X ITL2015 with BTV-25, 26, 27s and BTV XJ1407 and that serum of BTV-X ITL2015 infected goats failed to neutralise all tested extant serotypes, the existence of a novel BTV serotype circulating in goats in Sardinia can be proposed, it should be BTV-30, although not confirmed yet.

The three serotypes BTV-25, -26 and -27 are genetically grouped. Phylogenetic analyses with the 26 other established BTV serotypes revealed the closest relationship to BTV-25 (SWI2008/01) (80% nucleotide/86% amino acid) and to BTV-26 (KUW2010/02) (73–74 % nucleotide/80–81 % amino acid). However, highest sequence homologies between individual segments of BTV-27/FRA2014/v01–v03 with BTV-25 and BTV-26 vary. Neutralisation assays of anti-BTV27/FRA2014/v01–v03 sera with a reassortant virus containing the outer capsid proteins of BTV-25 (BTV1VP2/VP5 BTV25) further confirmed that BTV-27 represents a distinct BTV serotype.

## 3.2. Classification of existing strains

The output of the analysis as described in Section 3.2 is reported in Tables 1 and 2. Table 1 shows the data about pathogenicity (morbidity, mortality, case-fatality), epidemiological properties (transmission routes, host spectrum and no. of outbreak per week) and geographical spread for each BTV strains reported in Europe and neighbouring countries. Where data are not available is indicated (n.a.). In Table 2, the data from Table 1 are used to assess the spread capability to different episystem, speed of transmission, and pathogenicity score for the impact of BTV strains on cattle and small ruminants.

**Table 1:** Data about pathogenicity, epidemiological properties and geographical spread for each BTV strains reported in Europe and neighbouring countries are listed according to chronology of occurrence in the EU since 1999

| Serotype | Strains/ isolates | Countries | Episystem | Period | Host spectrum | Transmission route | Mean no. outbreak/ week (without vaccination) | Impact on small ruminants flocks | | | Impact on cattle herds | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | Median value of intra flock morbidity (5th, 95th percentile) | Median value of intra flock case fatality (5th and 95th percentile) | Median value of intra flock mortality (5th and 95th percentile) | Median value of intra herd morbidity (5th and 95th percentile) | Median value of intra flock herd fatality (5th and 95th percentile) | Median value of intra herd mortality (5th and 95th percentile) |
| BTV-4 | GRE1999/01 | EL, TR | SE | 1998–2001 | Cattle, SR | Vector-borne | 44.46 | 5.0% (0.7–30.8%) | 0.0% (0–100%) | 0.0% (0–10.0%) | n.a. | n.a. | n.a. |
| | SPA2003/01 SPA2004/01 IT2003/01 | ES, IT, FR (Corsica), MO, PT | SW | 2003–2005 | Cattle, SR | Vector-borne | 72.88 | 2.8% (0.3–20.8%) | 0.0% (0–66.7%) | 0.0% (0–2.6%) | n.a. | n.a. | n.a. |
| | MOR2009/07 | MO, ES, ALG, TU | SW | 2009–2012 | Cattle, SR | Vector-borne | n.a. | n.a. | n.a. | n.a. | n.a. | n.a. | n.a. |
| | IT2012/01 | IT (Sardinia) | SW | 2012 | Cattle, SR | Vector-borne | n.a. | n.a. | n.a. | n.a. | n.a. | n.a. | n.a. |
| | SPA2013/01 | ES, PT | SW | 2012–2013 | Cattle, SR | Vector-borne | n.a. | n.a. | n.a. | n.a. | n.a. | n.a. | n.a. |
| | CYP2011/01 | CY, IL, GR | SE | 2011–2013 | Cattle, SR | Vector-borne | n.a. | n.a. | n.a. | n.a. | n.a. | n.a. | n.a. |
| | GRE2014/07 IT2014/01 FR2016/01 | EL, ALB, BG, HR, RU, SE, SL, AT, IT, HU, MT, MK, FR (Corsica) | SE | 2014–2017 | Cattle, SR | Vector-borne | 63.99 | 5.8% (0.3–38.3%) | 25.0% (0–100%) | 1.0% (0–16.2%) | 2.7% (0–50%) | 0.0% (0–100%) | 0.0% (0–100%) |

| Serotype | Strains/ isolates | Countries | Episystem | Period | Host spectrum | Transmission route | Mean no. outbreak/ week (without vaccination) | Impact on small ruminants flocks | | | Impact on cattle herds | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | Median value of intra flock morbidity (5th, 95th percentile) | Median value of intra flock case fatality (5th and 95th percentile) | Median value of intra flock mortality (5th and 95th percentile) | Median value of intra herd morbidity (5th and 95th percentile) | Median value of intra flock herd fatality (5th and 95th percentile) | Median value of intra herd mortality (5th and 95th percentile) |
| BTV-1 | GRE2001/01 | EL | SE | 2001 | Cattle, SR | Vector-borne | 12.29 | 3.9% (0.8–18.4%) | 0.0% (0–66.7%) | 0.0% (0–4.6%) | n.a. | n.a. | n.a. |
| | SPA2007/04; FR2008/24 IT2006/01 | MO, ES, ALG, TU, IT (Sardinia), PT, FR | N/SW | 2006–2010 | Cattle, SR | Vector-borne | 108.42 | 10.0.% (0.4–100.0%) | 0.0% (0–80.0%) | 0.0% (0–5.2%) | 6.3% (0.7–100%) | 0.0% (0–0%) | 0.0% (0–0%) |
| | IT/2012/01 | IT | SW/SE | 2012–2014 | Cattle, SR | Vector-borne | 179.41 | 12.3.% (1.2–81.2%) | 26.9% (0–100%) | 3.8% (0–23.2%) | 4.8% (0.5–89.2%) | 0.0% (0–0%) | 0.0% (0–0%) |
| BTV-2 | IT2001/01 IT2001/03 FR2000/01 | TU, ALG, IT, ES (Balearic islands), FR (Corsica) | SW | 1999–2002 | Cattle, SR | Vector-borne | 200.90 | 1.8% (0.3–18.8%) | 0.0% (0–100%) | 0.0% (0–5.9%) | n.a. | n.a. | n.a. |
| BTV-9 | GRE1999/01 IT2000/01 IT2003/01 | TR, EL, IT, BG, MK, SE, BiH, ALB, HR | SE | 1999–2003 | Cattle, SR | Vector-borne | n.a. | n.a. | n.a. | n.a. | n.a. | n.a. | n.a. |

| Serotype | Strains/ isolates | Countries | Episystem | Period | Host spectrum | Transmission route | Mean no. outbreak/ week (without vaccination) | Impact on small ruminants flocks | | | Impact on cattle herds | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | Median value of intra flock morbidity (5th, 95th percentile) | Median value of intra flock case fatality (5th and 95th percentile) | Median value of intra flock mortality (5th and 95th percentile) | Median value of intra herd morbidity (5th and 95th percentile) | Median value of intra flock herd fatality (5th and 95th percentile) | Median value of intra herd mortality (5th and 95th percentile) |
| BTV-16 | GRE2000/01 | EL, TR | SE | 1999–2000 | Cattle, SR | Vector-borne | n.a. | n.a. | n.a. | n.a. | n.a. | n.a. | n.a. |
| | IT2002/01 | IT, IL | SE | 2002–2004 | Cattle, SR | Vector-borne | n.a. | n.a. | n.a. | n.a. | n.a. | n.a. | n.a. |
| | FR2004/01 IT2004/01 CRO2004 | IT, FR (Corsica), HR | SE | 2004 | Cattle, SR | Vector-borne | 2.27 | 1.7% (0.4–16.3%) | 0.0% (0–70%) | 0.0% (0–2.3%) | n.a. | n.a. | n.a. |
| | CY2004/01 CY2010/01 | CY | SE | 2003–2014 | Cattle, SR | Vector-borne | n.a. | n.a. | n.a. | n.a. | n.a. | n.a. | n.a. |
| BTV-8 | NL2006/04 | NL, BE, DE, FR, LU, DK, CZ, UK, ES, IT, NO, SW, CH, AT | N/SW | 2006–2009 | Cattle, SR | Vector-borne | 1,616.05 | 8.9% (0.4–100%) | 0.0% (0–100%) | 0.0% (0–17.0%) | 2.1% (0.4–100%) | 0.0% (0–0%) | 0.0% (0–0%) |
| | FR2015/01 | FR | N | 2015–2017 | Cattle, SR | Vector-borne | 53.84 | 3.0% (0.5–21.7%) | 0.0% (0–31.3%) | 0.0% (0–2.8%) | 0.9% (0.3–8.4%) | 0.0% (0–0%) | 0.0% (0–0%) |
| BTV-25 | CH2008/01 | CH, IT | SW | 2008–current | SR | Direct | n.a. | n.a. | n.a. | n.a. | n.a. | n.a. | n.a. |
| BTV-27 | FR2014/01 | F (Corsica) | SW | 2014–current | SR | Direct | n.a. | n.a. | n.a. | n.a. | n.a. | n.a. | n.a. |
| BTV-30 | IT2015/01 | IT (Sardinia) | SW | 2015–current | SR | Direct | n.a. | n.a. | n.a. | n.a. | n.a. | n.a. | n.a. |

BTV: bluetongue virus.
Episystems: Northern Europe (N), south-western Europe (SW), south-eastern Europe (SE).
Countries: Algeria (AL), Albania (AB), Austria (AT), Belgium (BE), Bulgaria (BG), Bosnia-Herzegovina (BiH), Switzerland (CH), Cyprus (CY), the Czech Republic (CZ), Germany (DE), Denmark (DK), Greece (EL), Spain (ES), France (FR), Croatia (HR), Hungary (HU), Israel (IL), Italy (IT), Luxemburg (LU), FYROM (MK), Morocco (MO), Montenegro (MT), the Netherlands (NL), Norway (NO), Portugal (PT), Romania (RU), Serbia (SE), Slovenia (SL), Sweden (SW), Turkey (TR), Tunisia (TU) and the United Kingdom (UK).

**Table 2:** Spread capability to different episystem, speed of transmission, and pathogenicity score for the impact of BTV strains on cattle and small ruminants

| Serotype | Strains/isolates | Spread capability to other episystem[a] | Level of transmissibility[b] | Pathogenicity score Small ruminants[c] | Pathogenicity score Cattle[d] |
|---|---|---|---|---|---|
| BTV-4 | GRE1999/01 | Yes | Low | 5 | n.a. |
| | SPA2003/01<br>SPA2004/01<br>IT2003/01 | | Medium | 4 | n.a. |
| | MOR2009/07 | | n.a. | n.a. | n.a. |
| | IT2012/01 | | n.a. | n.a. | n.a. |
| | SPA2013/01 | | n.a. | n.a. | n.a. |
| | CYP2011/01 | | n.a. | n.a. | n.a. |
| | GRE2014/07<br>IT2014/01<br>FR2016/01 | | Medium | 6 | 6 |
| BTV-1 | GRE2001/01 | Yes | Low | 5 | n.a. |
| | SPA2007/04;<br>FR2008/24<br>IT2006/01 | | Medium | 5 | 2 |
| | IT/2012/01 | | High | 6 | 2 |
| BTV-2 | IT2001/01<br>IT2001/03<br>FR2000/01 | No | High | 5 | n.a. |
| BTV-9 | GRE1999/01IT2000/01<br>IT2003/01 | No | n.a. | n.a. | n.a. |
| BTV-16 | GRE2000/01 | No | n.a. | n.a. | n.a. |
| | IT2002/01 | | n.a. | n.a. | n.a. |
| | FR2004/01<br>IT2004/01<br>CRO2004/01 | | Low | 4 | n.a. |
| | CY2004/01<br>CY2010/01 | | n.a. | n.a. | n.a. |
| BTV-8 | NL2006/04 | Yes | High | 6 | 2 |
| | FR2015/01 | | Medium | 3 | 1 |
| BTV-25 | CH2008/01 | Unknown | n.a. | n.a. | n.a. |

| Serotype | Strains/isolates | Spread capability to other episystem[(a)] | Level of transmissibility[(b)] | Pathogenicity score Small ruminants[(c)] | Pathogenicity score Cattle[(d)] |
|---|---|---|---|---|---|
| BTV-27 | FR2014/01 | Unknown | n.a. | n.a. | n.a. |
| BTV-30 | IT2015/01 | Unknown | n.a. | n.a. | n.a. |

BTV: bluetongue virus.
(a): The spread capability to other episystem is indicated on the basis of the data presented in Table 1, i.e. in how many episystems BTV strains of the same serotype have been reported (Yes: reported in more than one episystem; No: reported in only one episystem).
(b): Low = Mean no. outbreak/week < 50; Medium = Mean no. outbreak/week > 50 and < 150; High = Mean no. outbreak/week > 150.
(c): Pathogenicity score calculated as the sum of the following scores:

- intraflock morbidity > 15% = score 2; intraflock morbidity between 5% and 15% = score 1; intraflock morbidity < 5% = score 0.
- intraflock case-fatality rate > 50% = score 2; intraflock case-fatality rate between 20% and 50% = score 1; intraflock case-fatality rate < 20% = score 0.
- intraflock mortality > 10% = score 2; intraflock mortality between 3% and 10% = score 1; intraflock mortality < 3% = score 0.

(d): Pathogenicity score calculated as the sum of the following scores:

- intraherd morbidity > 4% = score 2; intraherd morbidity between 1% and 4% = score 1; intraherd morbidity < 1% = score 0.
- intraherd case-fatality rate > 50% = score 2; intraherd case-fatality rate between 20% and 50% = score 1; intraherd case-fatality rate < 20% = score 0.
- intraherd mortality > 1% = score 2; intraherd mortality between 0.5% and 1% = score 1; intraherd mortality < 0.5% = score 0.

From the analysis, it appears that all BTV strains belonging to the 'historical' serotypes (BTV- 1, -2, -4, -8 and -9) shown in Tables 1 and 2 are characterised by at least one strain with high level of virulence in at least one of the susceptible species, thus confirming the high variability of BTV in term of animal health impact according to the different biotic (e.g. host susceptibility, vector species and abundance) and abiotic conditions (climatic factors). A different case could be some strains belonging to serotype 16 where data are available for their current circulation in Italy (strain IT2004) and past circulation in Corsica and Croatia (FR2004 and CRO2004, Listeš et al., 2009), which are characterised by moderate, albeit variable, level of morbidity in small ruminants (median 1.7%; 0.4–16.3, 5th–95th percentiles), as well as case fatality, and very limited mortality rates, and speed of spread. However, experimental studies in naïve northern European sheep demonstrated that this virus serotype also has the capacity to be highly virulent, thus in line with what explained in Section 2.2 about the capacity of BTV serotype/strains to modify the virulence (Veronesi et al., 2010).

Small ruminant-adapted BTV strains belonging to serotypes BTV-25, -27, -30 and related isolates represent a novel group of the virus that is different from the biological and genetic point of view, they show very low or null level of virulence or pathogenicity; they have all been isolated in asymptomatic goats or sheep, and initial evidence indicates that they can be transmitted by contact rather than via vector insects.

Therefore the proposed grouping based on BTV strains as defined in the present opinion is:

- BTV strains belonging to serotypes BTV-1, -2, -4, -8, -9, that have circulated or are still circulating in some parts of Europe, as in Tables 1 and 2.
- Some strains of serotypes BTV-16 still circulating in some parts of Europe.
- Small ruminant-adapted strains (BTV strains belonging to serotypes BTV-25, -27, -30 and related isolates).

These groups are considered for the judgement on AHL criteria as in Sections 3.4, 3.5 and 3.6.

According to the assessment here presented, the only BTV serotypes that could be partially excluded from the overall BT policy currently in place in the EU, due to their low level of virulence or pathogenicity, are the small ruminant-adapted strains (serotypes BTV-25, -27, -30).

## 3.3. Assessment of BT serotype groups according to Article 7 criteria

This section presents the assessment of bluetongue according to the Article 7 criteria of the AHL and related parameters (see Table 2 of the opinion on methodology (EFSA AHAW Panel, 2017b)), based on the information contained in the fact sheet as drafted by the selected disease scientist (see Section 2.2 of the scientific opinion on the *ad hoc* methodology) and according to the serotype groups as mentioned in Section 3.2, the BTV strains belonging to serotypes BTV-1, -2, -4, -8, -9, -16 and the small ruminant-adapted strains (BTV strains belonging to serotypes BTV-25, -27, -30 and related isolates).

### 3.3.1. Article 7(a) Disease Profile

#### 3.3.1.1. Article 7(a)(i) Animal species concerned by the disease

*Susceptible animal species*

The information reported below is applicable to all BTV serotypes.

Parameter 1 – Naturally susceptible wildlife species (or family/orders)

The main vertebrate hosts of bluetongue virus are members of the Artiodactyla (even-toed ungulates).

Antibodies against BTV have been reported from a wide variety of other artiodactylids, including members of the Bovidae particularly a number of African antelope species; Cervidae and Camelidae as well as Giraffidae and *Antilocapra americana*. Less commonly, virus has been isolated from various species including several species of deer, and llamas, or viral RNA has been detected using reverse transcription polymerase chain reaction (RT-PCR). Given the broad range of species, potentially all ruminants and camelids can be infected. Further data concerning the range of species that are susceptible, including references, is available at Wildlife Information Network.[3]

Additionally, antibodies to BTV and in some cases viral RNA have also been detected in various carnivores (cats, dogs, other species), elephants and rhinoceros. BTV was isolated from several species

[3] http://wildpro.twycrosszoo.org/S/virus/reoviridae/ReoviridaeBTV/ReoviridaeBTV/03BTVSppDefinitiveHost_Mammals.htm

of rats, mice, voles, gerbils, etc. (family Muridae), *Rhabdomys pumilio* and *Otomys irroratus* in early work, and from a *Crocidura* sp. shrew.

The species that were found seropositive:

- White-tailed deer[4] , *Odocoileus virginianus*, Cervidae, Artiodactyla
- Brocket deer, *Mazama americana* and related species Cervidae, Artiodactyla
- Red deer[4], *Cervus elaphus,* Cervidae, Artiodactyla
- Wapiti elk, *Cervus canadensis,* Cervidae, Artiodactyla
- Roe deer, *Capreolus capreolus,* Cervidae, Artiodactyla
- Black-tailed deer, *Odocoileus hemionus*, Cervidae, Artiodactyla
- Axis deer, *Axis axis*, Cervidae, Artiodactyla
- Fallow deer, *Dama dama*, Cervidae, Artiodactyla
- Sika deer[2], *Cervus nippon*, Cervidae, Artiodactyla
- Musk deer, *Moschus moschiferus*, Cervidae, Artiodactyla
- Moose, *Alces alces,* Cervidae, Artiodactyla
- Reeve's muntjac*, Muntiacus reevesi,* Cervidae, Artiodactyla
- Bighorn sheep[4], *Ovis canadensis,* Bovidae, Artiodactyla
- Mouflon[4], *Ovis orientalis,* Bovidae, Artiodactyla
- Blesbuck, *Damaliscus albifrons*, Bovidae, Artiodactyla
- Blue wildebeest, *Connochaetes taurinus*, Bovidae, Artiodactyla
- Black wildebeest, *Connochaetes gnou*, Bovidae, Artiodactyla
- Buffalo, *Syncerus caffer,* Bovidae, Artiodactyla
- American bison (US: buffalo), *Bison bison,* Bovidae, Artiodactyla
- European bison/wisent, *Bison bonasus*, Bovidae, Artiodactyla
- Red hartebeest,[4] *Alcelaphus buselaphus*, Bovidae, Artiodactyla
- Impala[4], *Aepyceros melampus*, Bovidae, Artiodactyla
- Common eland, *Taurotragus oryx*, Bovidae, Artiodactyla
- Arabian oryx, *Oryx leucoryx,* Bovidae, Artiodactyla
- Addax, *Addax nasomaculatus*, Bovidae, Artiodactyla
- Nubian ibex, *Capra nubiana,* Bovidae, Artiodactyla
- Sable antelope[4], *Hippotragus niger*, Bovidae, Artiodactyla
- Springbok, *Antidorcas marsupialis,* Bovidae, Artiodactyla
- Pronghorn, *Antilocapra americana*, Bovidae, Artiodactyla
- Musk ox, *Ovibos moschatus*, Bovidae, Artiodactyla
- Alpine ibex, *Capra ibex*, Bovidae, Artiodactyla
- Siberian ibex, *Capra sibirica*, Bovidae, Artiodactyla
- Spanish ibex, *Capra pyrenaica*, Bovidae, Artiodactyla
- Blackbuck, *Antilope cervicapra*, Bovidae, Artiodactyla
- Greater kudu[4], *Tragelaphus cubensis*, Bovidae, Artiodactyla
- Giraffe, *Giraffa camelopardalis*, Giraffidae, Artiodactyla
- Okapi[4], *Okapia johnstoni*, Giraffidae, Artiodactyla
- Collared peccary, *Pecari tajacu,* Tayassuidae*,* Artiodactyla
- White rhinoceros, *Ceratotherium simum,* Rhinocerotidae, Perissodactyla
- Black rhinoceros, *Diceros bicornis,* Rhinocerotidae, Perissodactyla
- African elephant, *Loxodonta africana*, Elephantidae, Proboscidea
- Asian elephant, *Elephas maximus,* Elephantidae, Proboscidea
- Cheetah, *Acinonyx jubatus*, Felidae, Carnivora
- Lion, *Panthera leo*, Felidae, Carnivora
- Eurasian lynx, *Lynx lynx,* Felidae, Carnivora
- Florida panther, *Puma concolor coryi,* Felidae, Carnivora
- African wild dog, *Lycaon pictus,* Canidae, Carnivora
- Spotted hyena, *Crocuta crocuta*, Canidae, Carnivora
- Jackal, *Canis mesomelas,* Canidae, Carnivora
- Large spotted genet (*Genetta tigrina*), Viverridae, Carnivora
- Black bear, *Ursus americanus floridanus,* Ursidae, Carnivora.

[4] Clinical disease has been also reported in this species.

Parameter 2 – Naturally susceptible domestic species (or family/orders)

Among the most common domestic ruminant species bred in the EU, it is generally considered that *Ovis aries* (domestic sheep) are the main clinically affected species while *Bos taurus* (domestic cattle) can be infected but rarely showing the clinical disease. *Capra hircus* (domestic goat) also can be infected. Current data suggests that at least some strains of the novel serotypes (particularly BTV-25) may show specificity for goats (Hofmann et al., 2008). Other domestic species found seropositive for BTV include:

- Water buffalo, *Bubalus bubalis*, Bovidae, Artiodactyla
- One-humped camel, *Camelus dromedarius*, Camelidae, Artiodactyla
- Bactrian camel, *Camelus bactrianus*, Camelidae, Artiodactyla
- Alpaca, *Vicugna pacos*, Camelidae, Artiodactyla
- Llama, *Lama glama*, Camelidae, Artiodactyla
- Yak, *Bos grunniens*, Bovidae, Artiodactyla (also clinical disease detected)
- Domestic dog, *Canis familiaris*, Canidae, Carnivora
- Domestic cat, *Felis catus*, Felidae, Carnivora

Parameter 3 – Experimentally susceptible wildlife species (or family/orders)

- American bison, *Bison bison*, Bovidae, Artiodactyla
- Black-tailed deer, *Odocoileus hemionus*, Cervidae, Artiodactyla
- White-tailed deer, *Odocoileus virginianus*, Cervidae, Artiodactyla
- Red deer, *Cervus elaphus,* Cervidae, Artiodactyla
- Wapiti elk, *Cervus canadensis*, Cervidae, Artiodactyla
- Pronghorn antelope, *Antilocapra americana*, Bovidae, Artiodactyla
- African buffalo, *Syncerus caffer*, Bovidae, Artiodactyla

Parameter 4 - Experimentally susceptible domestic species (or family/orders)

- Cattle, *Bos taurus*, Bovidae, Artiodactyla
- Goat, *Capra hircus*, Bovidae, Artiodactyla
- Sheep, *Ovis aries*, Bovidae, Artiodactyla
- Alpaca (*Vicugna pacos*) (Schulz et al., 2012)
- Llama (*Lama glama*), Camelidae, Artiodactyla

*Reservoir animal species*

Since in most outbreaks BT is a vector-borne disease (except for serotypes 25–27, which can be directly transmitted), the level of viraemia and its duration are key factors for a host to be a reservoir. Prolonged but not persistent cell-associated viraemia is characteristic of BTV infection of ruminants (Barratt-Boyes and MacLachlan, 1995; MacLachlan, 2004), and plasma viraemia is transient and of relatively low titre, while adult *Culicoides* become infected for life.

This prolonged blood cell-associated infection of ruminants is important, because it increases the likelihood that feeding insect vectors will acquire infection, and prolonged infection also potentially complicates the safe movement of animals between BTV-free and -infected regions. Although it is clear that BTV infection of ruminants is prolonged but not persistent (MacLachlan, 2004; Melville et al., 2004; White and Mecham, 2004; Lunt et al., 2006), the reported duration of viraemia in ruminants has varied markedly between studies.

An animal species can be classified as reservoir for BTV if it maintains the virus in the field, acting as a source of infection, and further spread, in the presence of other favourable factors: climatic conditions and related presence and abundance of vectors, density of susceptible wild and domestic host population.

Recent studies indicate that at least for BTV-1–24 the duration of viraemia in BTV-infected ruminants reflects in part the life span of circulating red blood cells that carry the virus, thus viraemia is slightly longer in cattle than in sheep infected with the same strain of BTV as the life span of red blood cells is somewhat longer in cattle than it is in sheep, (Bonneau et al., 2002). It is important to note that although the virus is attached to red blood cells via its haemagglutinin activity, and its genomic RNA can be detected by diagnostic molecular techniques (for example RT–PCR assays), it progressively becomes more difficult to recover infectious virus in cell cultures or other systems. After the initial period of viraemia (and circulation of infectious virus) lasting 3–4 weeks, the level of neutralising antibodies increases to the point where virus isolation is difficult or not feasible. The

animals involved can therefore be considered as non-infectious, even though viral genome RNA may still be detectable in some animals for extended periods. Comparison of data obtained from prior studies is further complicated by the fact that these studies have described infections with a variety of BTV serotypes and strains, animals of different ages and breeds that were either naturally or experimentally infected with BTV (by different routes of inoculation), and different methods of virus isolation or detection (Singer et al., 2001). The virus inoculum used in each study is especially important, not just because of the potential impact of genetic variations between strains and serotypes, but also because of the biological properties of field (wild-type) and laboratory-adapted strains of BTV can be markedly different (Kirkland, 2004; Kirkland and Hawkes, 2004).

In the past decade, new serotypes (BTV-25, BTV-26, BTV-27 and related strains) have been described (Hofmann et al., 2008; Maan et al., 2011c; Zientara et al., 2014; Savini et al., 2017). These differ from the historical 24 serotypes, because they are characterised by causing asymptomatic infections, at least for BTV-26 (Batten et al., 2014), they have longer viraemia, suggesting an alternative mechanism of persistence in the host (BTV-25, Vogtlin et al., 2013) and use goats and sheep as reservoir hosts (Batten et al., 2012, 2013a). They are therefore defined in the current opinion as 'small ruminant-adapted strains'. Furthermore there is evidence that these novel strains cannot infect (at least one) known vector species of biting midge, *Culicoides sonorensis* since do not infect a *C. sonoresis* cell line, or colony-derived adult insects via an oral route (Pullinger et al., 2016). However, there are no data concerning the ability of the small ruminant-adapted novel strains to infect European vectors. These data suggest that, for at least for the novel serotypes, direct contact may be the primary route of transmission.

Parameter 5 – Wild reservoir species (or family/orders)

In Table 3 below, further information on length of viraemia in the wild reservoir species for different BTV serotypes is reported. Out of those species, red deer could be a possible wild reservoir of BTV in the EU (EFSA AHAW Panel, 2017a).

**Table 3:** Summary outcomes of systematic review of experimental infections with BTV in wild species (papers published up to January 2016)

| Common name | Species | Family | Order | Ref | BTV serotype | Virus detection (range of days) | |
|---|---|---|---|---|---|---|---|
| | | | | | | Virus isolation | RT-PCR |
| Alpaca | *Vicugna pacos* | Camelidae | Artiodactyla | Schulz et al. (2012) | 8 | 2–6 | 2–35 (106) |
| American bison | *Bison bison* | Bovidae | Artiodactyla | Tessaro and Clavijo (2001) | 11 | 4–42 | |
| Camel | *Camelus dromedarius* | Camelidae | Artiodactyla | Batten et al. (2011) | 1 | 7–8 | 5–68 |
| Deer (Mule, White-tailed and Red deer) | *Odocoileus hemionus, Odocoileus virginianus, Cervus elaphus* | Cervidae | Artiodactyla | Work et al. (1992), Drolet et al. (2013), Thomas and Trainer (1970), Vosdingh et al. (1968), Lopez-Olvera et al. (2010), Lorca-Oro et al. (2012) | 1, 8, 10, 17 | 2–28 | 1–112 |
| Llama | *Lama glama* | Camelidae | Artiodactyla | Schulz et al. (2012) | 8 | 2–6 | 2–35 (106) |
| Wapiti elk | *Cervus canadensis* | Cervidae | Artiodactyla | Murray and Trainer (1970), Stott et al. (1982) | 8,11 | 2–10 (190 bone marrow) | |

Parameter 6 – Domestic reservoir species (or family/orders)

In a previous EFSA opinion, based on a systematic literature review, it was concluded that, in general for all BTV serotypes, BTV nucleic acid can be detected by RT-PCR in the blood of infected cattle and sheep for 4–5 months after the infection, and up to 2 months in goats, while infectious virus in the blood can only be detected for up to 50 days in cattle and up to 30 days in small ruminants in the majority of the cases (EFSA AHAW Panel, 2017a).

In Table 4 below, further information on length of viraemia in the three main domestic ruminant species about different BTV serotypes is reported.

**Table 4:** Summary outcomes of systematic review of experimental infections with BTV in domestic species (papers published up to January 2016)

| Common name | Species | Ref | No of Animals | BTV serotype | Virus detection (range of days) | |
|---|---|---|---|---|---|---|
| | | | | | Virus isolation | RT-PCR |
| Cattle | *Bos taurus* | Anderson et al. (2014), Backx et al. (2009), Barratt-Boyes and MacLachlan (1994), Barratt-Boyes et al. (1995), Barros et al. (2009), Bonneau et al. (2002), Bowen and Howard (1984), Bowen et al. (1983), De la Concha-Bermejillo et al. (1993), Darpel et al. (2016), DeMaula et al. (2002), Ellis et al. (1993), Groocock et al. (1983), Gu et al. (2014), Gubbins et al. (2012), Hamers et al. (2009a), Jochim et al. (1974), Luedke et al. (1969), MacLachlan and Fuller (1986), MacLachlan and Thompson (1985), MacLachlan et al. (1994, 1984, 1987, 1990), Martinelle et al. (2011), Monaco et al. (2004a,b,c), Odeon et al. (1999), Parsonson et al. (1994, 1987a,b), Dal Pozzo et al. (2009), Richards et al. (1988), Roeder et al. (1991), Schlafer et al. (1990), Van der Sluijs et al. (2012), Squire (1989), Thomas et al. (1985), Waeckerlin et al. (2010), Waldvogel et al. (1992a); Waldvogel et al. (1992b), Whetter et al. (1989) | 350 | 1, 2, 4, 8, 10, 11, 17, 20 | 1–62 | 1–167 |
| Goats | *Capra hircus* | Batten et al. (2014, 2012), Belbis et al. (2013), Breard et al. (2011), Caporale et al. (2014), Coetzee et al. (2013), Planzer et al. (2011), Vogtlin et al. (2013) | 12 | 4, 8, 25, 26 | 3–32 | 2–55 |

| Common name | Species | Ref | No of Animals | BTV serotype | Virus detection (range of days) | |
|---|---|---|---|---|---|---|
| | | | | | Virus isolation | RT-PCR |
| Sheep | *Ovis aries* | Anderson and Jensen (1969), Backx et al. (2007), Batten et al. (2012), Bonneau et al. (2002), Breard et al. (2015), Caporale et al. (2014), Chaignat et al. (2009), Chand et al. (2009), Channappanavar et al. (2012), Darpel et al. (2016), DeMaula et al. (2002), Dungu et al. (2008), Ellis et al. (1993), Emidio et al. (2004), Enright and Osburn (1980), Eschbaumer et al. (2010, 2009), Feenstra et al. (2014), Flanagan et al. (1982), Forman et al. (1989), van Gennip et al. (2012), Ghalib et al. (1985), Goldsmit et al. (1975), Gubbins et al. (2012), Hamblin et al. (1998), Hamers et al. (2009a,b), Hare et al. (1988), Jeggo et al. (1987), Koumbati et al. (1999), Letchworth and Appleton (1983), Luedke (1969), Luedke et al. (1976, 1969), Lunt et al. (2006), MacLachlan et al. (2008), Mahrt and Osburn (1986), Matsuo et al. (2011), McColl and Gould (1994), Moulin et al. (2012), Nunamaker et al. (1992), Pages et al. (2014), Pini (1976), Ramakrishnan et al. (2006), Rasmussen et al. (2013), Richards et al. (1988), Richardson et al. (1985), Sanchez-Cordon et al. (2013), Savini et al. (2007), Shad et al. (1997), Singh et al. (2008), Van der Sluijs et al. (2011, 2012, 2013a, 2013b), Squire (1989), Stanislawek et al. (1996), Stott et al. (1985), Tanya et al. (1992), Tessaro and Clavijo (2001), Tomori (1980), Umeshappa et al. (2011), Uren and George (1985), Uren and Squire (1982), Veronesi et al. (2010), Waeckerlin et al. (2010), Worwa et al. (2010) | 1,108 | 1, 3, 4, 7, 8, 9, 10, 11, 13, 14, 16, 17, 18, 2, 20, 21, 23, 25, 26 | 1–54 | 1–222 |

#### 3.3.1.2. Article 7(a)(ii) The morbidity and mortality rates of the disease in animal populations

*Morbidity*

Parameter 1 – Prevalence/Incidence

In the course of a BTV infection in a region, three fundamental steps can be distinguished (Randolph and Rogers, 2010): introduction, establishment and spread in a geographical sense. A fourth period may be seen after an outbreak, where, although there are still sources of infection, much of the ruminant population may be immune and the number of new cases is very low. During this period, the outbreak may become self limiting and can disappear. This may explain why many outbreaks of BT caused by a single serotype last for 3 years. During these different stages, the prevalence of infected animals in a region changes, since, upon introduction into a BTV-free region, the prevalence in a geographical unit rises from zero to a maximum (plateau prevalence) and subsequently drops again either to zero, in case the infection fades out, or to a level determined by endemic infection in the region (Giovannini et al., 2004; Schaik et al., 2008; Santman-Berends et al., 2010; EFSA AHAW Panel, 2017a). The value of the plateau prevalence depends on the density of susceptible ruminants, the relative efficiency of transmission of the virus strain involved and the

density of active and competent vectors (Hartemink et al., 2009) and the contact pattern between them. Whether the virus is able to establish an endemic infection in the area depends on the ability of the virus to overwinter and the rate at which susceptible ruminants are re-introduced into the population (vaccination reduces this rate).

The infection and serological prevalence values (virus and antibody prevalence) at herd and animal level obtained from a SLR and from the MSs are reported in previous EFSA outputs (EFSA AHAW Panel, 2017a), where information at serotype level is available only for BTV-8. In the epidemiological phase 3 (infection population with prevalence having reached a plateau), the seroprevalence at animal level ranged from 1.1% to 99% (median 38%) (data from SLR), and from 0.023% to 100% with median value of 24% (data from MSs). The virus prevalence ranged from 0.1% to 9% with median value of 1.6% (data from SLR).

Parameter 2 – Case-morbidity rate (% clinically diseased animals out of infected ones)

Disease severity may be influenced by factors such as the virus strain, host factors (e.g. level of immunity (including colostral antibodies), to the same or to heterologous serotypes, general health, genetic factors, age and possibly breed) and environmental stressors. Sheep are usually the most severely affected domesticated species, and in endemic regions, they are often the only domesticated animal with obvious clinical signs. Morbidity rates in sheep range from < 5% to 50–75% (or higher), and are usually at their highest when the virus is first introduced (CSFPH, 2015). Once a virus has become endemic, morbidity may decrease to low levels (e.g. 1–2%), with very few deaths. The introduction of an exotic strain into an endemic region may also result in a new outbreak of disease with high levels of morbidity and mortality. Outbreaks are uncommon where a virus circulates year-round. Other species such as cattle and goats can also be affected when a bluetongue virus is introduced into a naive population. Cattle became ill during recent serotype 8 and 4 outbreaks in Europe.

Information on different levels of morbidity for different BTV strains is shown in Table 1, based on ADNS data since 1999. As shown, morbidity of BT can be very variable even within the same serotype, but all 'historical' serotypes were categorised in the impact table as high virulent (pathogenicity score 5 and 6) at least for one strain. On the contrary, the novel small ruminant-adapted strains (belonging to BTV-25, -26, -27) do not cause significant clinical symptoms. In order to show this variability, the boxplot displaying the distribution of the within-herd morbidity in sheep and cattle for as examples, the outbreak of BTV-4 in 2014–2016 and BTV-8 in 2006–2009 is shown in Figures 1 and 2.

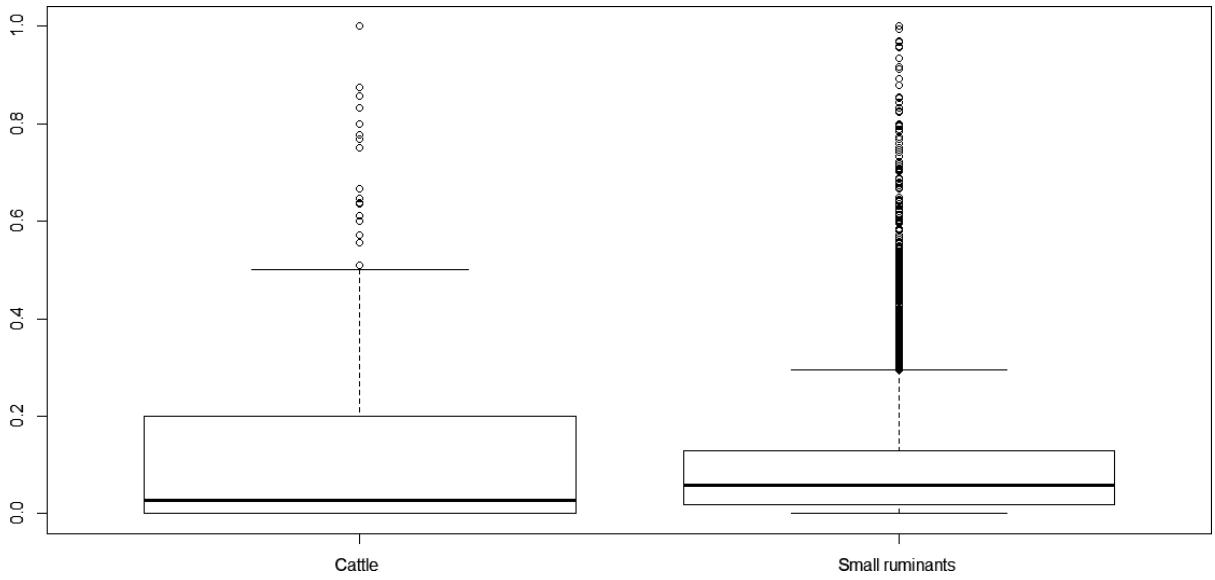


**Figure 1:** Intraherd morbidity of BTV-4 in small ruminants and cattle in the epidemics 2014–2016

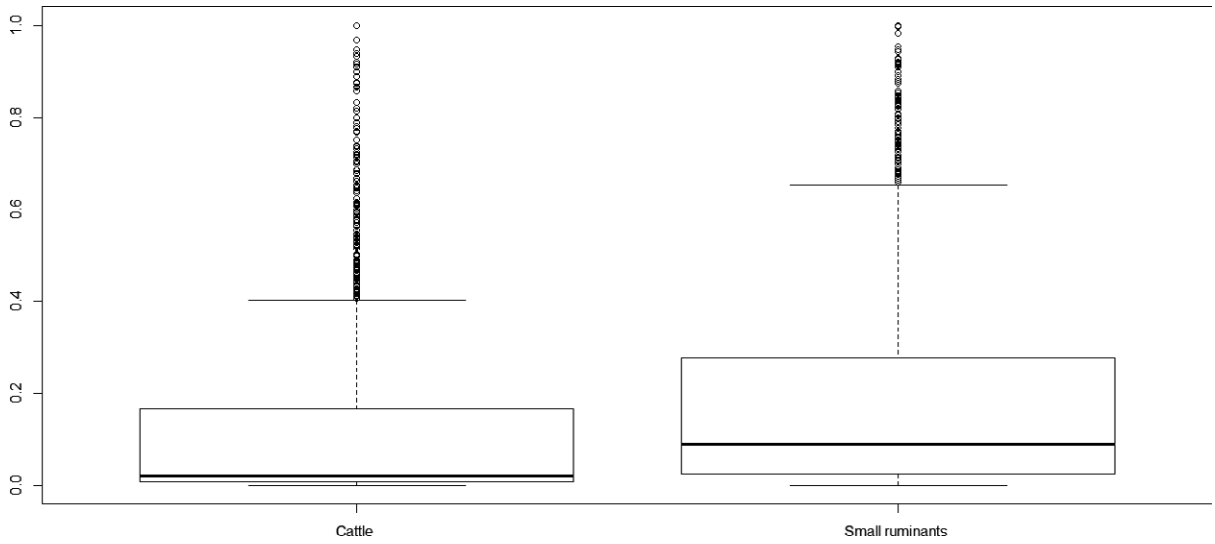


**Figure 2:** Intraherd morbidity of BTV-8 in small ruminants and cattle in the epidemics 2006–2009

This extreme high variability in morbidity and mortality rates is generally and globally recognised for all 'classical' serotypes, as reported by the OIE both in the technical disease card on bluetongue: 'Morbidity in sheep can reach 100% with mortality between 30% and 70% in more susceptible breeds; mortality in wild deer and antelopes can reach 90%'. (OIE, 2013b), and in the OIE manual where it is stated that the outcome of infection ranges from unapparent in the vast majority of infected animals, especially wild African ruminants, cattle and goats, to serious or fatal in a proportion of infected sheep, goats, deer and some wild ruminants, although higher incidence of clinical disease has been observed in cattle infected with BVT-8 in Europe (OIE, 2017). Furthermore some breeds of sheep are more susceptible to disease than others: clinical signs of disease in sheep vary markedly in severity, influenced by the type or strain of the infecting virus, husbandry factors as well as by breed (OIE, 2017).

Even in endemic countries BTV epidemics supported by particularly favourable climatic and environmental condition can cause extensive losses. For example, in India, BT caused death of 300,000 sheep and goats in Tamil Nadu during the monsoon season of 1997–1998 and repeated epidemics were observed in the following years (Ranjan et al., 2015)

Also, the literature on BT outbreaks in Europe confirms this characteristic of extreme variability of the clinical outcome of BTV infection. Within the same sheep breed, or even within the same flock,

there may be considerable differences in the severity of the disease occurrence in individual animals. Serotypes/strains of BTV with different degrees of virulence have been described in the literature For example, the North European BTV-8 strains that spread since 2006 in northern Europe is considered highly virulent, as it induced severe clinical disease in cattle and in naive sheep. On the other hand, it is interesting to note that no clinical cases of disease were observed even in sheep when BTV-8 reached northern Italy and Sardinia a few years later (Caporale et al., 2014).

During the first BTV-2 epidemics in Italy in 2000–2001 (Calistri et al., 2004a), in absence of any vaccination intervention, approximately 263,000 diseased sheep and goats were reported (18% morbidity) and 48,000 sheep and goats died (3% mortality). During the second BTV-2 epidemic in 2001–2002, approximately 251,000 diseased sheep and goats were reported (18% morbidity) and 73,000 sheep and goats died (5% mortality).

In the recent BT epidemic in south-east Europe linked to BTV-4, in Greece in 2014, a total of 2,895 outbreaks have been reported with morbidity rates of 11.0%, 2.0% and 3.5%, in sheep, goats and cattle, respectively. However in field investigations, a significantly higher bluetongue morbidity rate (27.5%) in sheep was reported (Vasileiou et al., 2016). In another survey on 15 sheep flocks, the average morbidity of BT in the sheep flocks was estimated to be 15.3% (95% CI 6.8–23.8%) and the average mortality and case fatality were 4.5% (95% CI 1.5–7.6%) and 32.0% (95% CI 18.1–42.9%), respectively (Katsoulos et al., 2016). The BTV seroprevalence and the ratio of clinical manifestations-to-infections determined in seven of these flocks, were on average 36.5% (95% CI 15.7–57.3%) and 24.6% (95% C.I. 12.8–36.3 %), respectively (Katsoulos et al., 2016).

In Romania, in 2014, the overall observed morbidity rate considering the whole outbreak period from August to December was 0.05% in cattle and 0.03% in sheep, but with peaks of 43% in cattle and 3.8% in sheep at the beginning of the outbreak (Tilibaşa et al., 2014). In Serbia, the same BTV-4 epidemics caused economic losses affecting sheep, cattle and goats with morbidity of 0.2%, 0.06% and 0.03%, respectively. Recorded mortality in cattle, sheep and goats was 18.45% (n = 38), 48.10% (n = 1,002) and 54.17% (n = 13), respectively (Djurić et al., 2017).

The same situation of variable clinical impact of BT has been observed in Spain, which has been affected by several different BTV serotypes in the last 50 years. In the review by Diego et al. (2013), who reviewed the history of BT epidemics in Spain since the 1960s, it was confirmed that BT outbreaks have shown variable clinical signs, morbidity and mortality. In the 1960s, morbidity in sheep due to BTV-10 outbreak was 3.5% and mortality 2.6%. This serotype caused disease in approximately 180,000 animals in the Spanish epidemic. The outbreak of BTV-2 in Balearic Islands in 2,000 led to the death of approximately 10,000 animals, due to the disease or stamping out, with a morbidity of 14.1% and mortality of 7.8%. With the first report of BTV-4 in 2004, which spread rapidly throughout southern Spain, 332 outbreaks were reported but no clinical disease was observed in bovines, and low morbidity and mortality were reported in sheep. Later on, in 2007, BTV-1 was detected which caused an average mortality of 7%, and proven to be more virulent than BTV-4 for the Spanish sheep. In 2008, BTV-8 strain was detected for the first time in northern Spain, which caused only mild clinical disease in sheep, in contrast to the more serious disease observed elsewhere in northern Europe (Diego et al., 2013).

For example, the outbreaks due to BTV-8 in sheep in the Netherlands in 2006 caused 7.7% morbidity and 4.4% mortality (Elbers et al., 2008). In Germany, in the same epidemics, morbidity was 2.3% and 6.3%, mortality of 0.2% and 2.6%, and a case-fatality rate of 6.4% and 37.5% in 2006 and 13.1% and 41.5% in 2007, in cattle and sheep respectively.

Among wildlife, white-tailed deer, brocket deer and pronghorn antelope can be severely affected, with morbidity rates reported to be as high as 100%. In Europe, red deer seem to be the most important wildlife species; during BTV-8 outbreaks, more than half the red deer surveyed in some areas were seropositive. A few seropositive dogs have been reported in the USA and a pair of Eurasian Lynx died after becoming infected with BTV-8 after ingesting infected meat (Jauniaux et al., 2008). Sanderson (2012) reported seropositivity to BTV-8 in the following ruminant species from European zoos: yak (*Bos grunniens*), American Bison (*Bison bison*), European bison (*Bison bonasus*), blackbuck (*Antilope cervicapra*), mouflon (*Ovis orientalis*), ibex (*Capra ibex*), Siberian ibex (*Capra sibirica*), musk ox (*Ovibos moschatus*), alpaca (*Lama pacos*), Bactrian camel (*Camelus bactrianus)*, fallow Deer (*Dama dama*). In over 200 African ruminant species from European zoos, different level of seropositivity was detected, although none of them showed clinical signs, being consistent with the observation in the field where indigenous antelope do not develop any clinical symptoms (Sanderson et al., 2012).

*Mortality*

Parameter 3 – Case-fatality rate

Information on different levels of mortality (number of deaths out of the total susceptible population) and case-fatality rates (proportion of deaths out of infected cases) in different BTV strains is shown in the Table 1, based on ADNS data since 1999 and in the above section on case-morbidity rate when discussing literature findings on different BT outbreaks. The case-fatality is very variable, even within the same serotype, and depending on the immune status of the host can vary dramatically even with the same virus strain, but all 'historical' serotypes (BTV-1–9) were categorised in the impact table as highly lethal above all for sheep (cattle and goats it is generally lower and may be negligible), up to 100% (given the worst case, 95th percentile of the distribution) at least for one strain within the same serotype. In contrast, the small ruminant adapted strains (BTV-25–30) are not considered to cause any significant clinical symptoms. BTV-16 has lower mortality rates during recent circulation in southern Europe.

The case fatality rate is typically < 30%, can reach 50–90% in highly susceptible populations, and decrease to very low levels once the virus has become endemic (CSFPH, 2015). Case-fatality can vary with the strain of BTV, host species, immune status and breed infected. It has also been reported that different populations of the same sheep breed from different regions can have different levels of innate resistance to specific virus strains. Local sheep breeds can also show higher levels of resistance to indigenous virus strains, but may be severely affected by introduced exotic strains. Mortality and case fatality is likely to be highest when a strain of BTV reaches an area for the first time.

An incursion in 2001 of BTV-2 into Corsica caused a mortality of 40% in unvaccinated sheep flocks. This was compared with 5.1% in vaccinated flocks (Breard et al., 2004). More recently, in Corsica with the outbreak of BTV-1 in 2013, morbidity and mortality rates on the day of notification varied from 1% to 80% and 0% to 11%, respectively, depending on the herds. (Sailleau et al., 2015).

Giovannini et al. (2004) reported a mortality rate among sheep and goats of 3.3% when BTV-2 occurred in Sardinia, Sicily and Calabria in 2000. The following year a more widespread epidemic mainly due to BTV-9 was associated with a mortality of 5.2%.

A study from the Netherlands was based on official reports from farms to estimate the mortality in cattle attributable to the BTV-8 epidemic in 2007 (Santman-Berends et al., 2011b). In confirmed infected herds, they reported a mortality rate ratio of between 1.2 (95% CI 1.1–1.3), 1.3 (95% CI 1.1–1.5), and 1.4 (95% CI 1.2–1.6) for age categories < 3 days, 3 days–1 year and > 1 year, respectively. This estimate was based on a comparison between BTV-8 affected months and non-affected months in the same herd adjusted for relevant confounders.

In Germany, BTV-8 in 2006–2007 led to a case-fatality rate of 37–41% in sheep, 6–13% in cattle and 26% in goats (Conraths et al., 2009).

In wild animals, Sanderson (2012) reported mortality linked to BTV infection in ruminant species from European zoos, same species as indicated in section about case-morbidity. Furthermore, in the US, Thorne et al. (1988) reported 2.3% mortality in pronghorn (*Antilocapra americana*), and less than 1% in mule deer (*Odocoileus hemionus*) and white-tailed deer (*Odocoileus virginianus).*

#### 3.3.1.3. Article 7(a)(iii) The zoonotic character of the disease

Humans are not susceptible to bluetongue virus.

#### 3.3.1.4. Article 7(a)(iv) The resistance to treatments, including antimicrobial resistance

Not applicable, since antiviral treatment is not used against BTV as feasible control option.

#### 3.3.1.5. Article 7(a)(v) The persistence of the disease in an animal population or the environment

*Animal population*

There are currently 27 confirmed serotypes of BTV, with additional strains that have been identified that may represent a total of > 30 serotypes (Maan et al., 2011c, 2012a,b; Zientara et al., 2014; Savini et al., 2017). The global distribution of these serotypes is not uniform, rather different constellations of BTV serotypes are disseminated by different species of *Culicoides* vector in relatively distinct global ecosystems (Gibbs and Greiner, 1994; Daniels et al., 2004; Maclachlan and Osburn, 2006; Tabachnick, 2004). BTV serotypes 25–27 have been identified only recently as infecting small ruminants in Europe and the Middle East, and serotype 25 (BTV-25; also known as Toggenburg orbivirus) has yet to be

isolated although it has been sequenced (Maan et al., 2011c; Zientara et al., 2015; 36). While the epidemiologic features of BTV-1–24 infections are similar in that they are all spread predominantly by biting *Culicoides* midges, there is uncertainty regarding the role of *Culicoides* midges (if any) in the transmission of BTV-25, BTV-26 and BTV-27 (Vogtlin et al., 2013; Batten et al., 2014). Duration of viraemia in BTV-25 infected goats also is markedly more prolonged than that in livestock infected with other BTV serotypes (Singer et al., 2001; Verwoerd and Erasmus, 2004; Maclachlan et al., 2009; OIE, 2013a; Vogtlin et al., 2013).

For those serotypes (1–24) of BTV which use haematophagous vectors for transmission, the level of viraemia and its duration are key factors for virus transmission. Studies with recent European isolates of BTV serotypes 2, 4, 9 and 16 established viraemia periods of 14–45 days in experimentally infected sheep (longest in sheep inoculated with serotype 2), up to 31 days in goats inoculated with serotype 2 and up to 19 days in cattle inoculated with serotype 2 or 4 (Savini et al., 2001; Monaco et al., 2006; Savini et al., 2006a,b). Viraemia persisted in sheep vaccinated with live attenuated strains of BTV-2, -4, -9 and -16 (including multivalent constructs) for up to 24 days, whereas viraemia in cattle inoculated with the same live attenuated vaccine viruses persisted for up to 78 days (Monaco et al., 2004a,b, 2006; Savini et al., 2004a,b, 2005a,b, 2006c). The recent output by EFSA showed that BTV nucleic acid can be detected by RT-PCR in the blood of infected cattle and sheep till 4–5 months after the infection, and up to 2 months in goats, while infectious virus in the blood can only be detected for up to 50 days in cattle and up to 30 days in small ruminants in the majority of the cases (EFSA AHAW Panel, 2017a).

This approximately 60-day infective period is considerably shorter than the interval (up to 7 months or even longer) after infection of ruminants when BTV nucleic acid may be detected in ruminant blood by appropriate prescribed BTV-specific PCR assays (MacLachlan et al., 1994; Bonneau et al., 2002). Since PCR detects BTV RNA but cannot distinguish between inactivated and infectious virus, the PCR assay is overly sensitive for identifying animal that still represent a source of BTV infection, but is useful for detecting those animals that have been infected, but are no longer a source of infection, for surveillance purposes. A 60-day infective period is more reflective of the maximal period when ruminants are thought to be infectious to competent insect vectors, although in reality the duration of this 'infectivity' is also affected by the level of viraemia in the host (which determines the amount of virus ingested by the insect and consequently the percentage of insects that become infected) which gradually declines, and consequently, the highest probability 'infectious period' is markedly shorter than 60 days, in the vast majority of infected ruminants. During this period, the infected host will normally develop a neutralising antibody response, which in itself is considered likely to reduce the possibility of circulating virus being infectious. However, authentic instances of individual animals with viraemias of greater than 60 days have been described on occasion in naturally infected cattle (Owen et al., 1965; Melville et al., 1996), and may be a feature of infection with certain strains of specific BTV serotypes (e.g. serotypes 15 and 16) and inoculation with certain live attenuated vaccine virus strains (Monaco et al., 2004a,b,c).

The OIE accepted and adopted an infective period of 60 days for BTV-infected ruminants, after due discussion and consideration of all published data. Prolonged viraemia has also been reported in other species, such as red deer (*Cervus elaphus*). The epidemiology of BTV-25, BTV-26 and BTV-27 infection of goats appears to be different than that of the other serotypes (BTV-1–24) and may not involve *Culicoides* midges (Vogtlin et al., 2013). Recent studies also suggest direct contact transmission of BTV-26, likely by aerosol, between goats (Batten et al., 2014). In one report, serotype 25 viral RNA was found for at least 2 years in goats, and the blood of some animals was infectious at 12–19 months (Vogtlin et al., 2013).

*Environment*

Parameter 4 – Length of survival (dpi) of the agent and/or detection of DNA in selected matrices (soil, water, air) from the environment (scenarios: high and low T)

BTV can remain viable in infected tissue or blood samples for many years when stored refrigerated at 4°C or frozen at −70°C (Parsonson and McColl, 1995). In a systematic review of literature on vector-borne pathogens, only one reference was found reporting survival times for BTV (Parsonson and McColl, 1995). In this study, sheep were inoculated with BTV serotypes 1, 11, 17 and 23, and samples were collected at necropsy and stored at −70°C for 1,277 or 5,110 days. Infectious virus samples have been stored and recovered from the orbivirus reference collection[5] after 30 years at −80°C.

[5] http://www.reoviridae.org/dsRNA_virus_proteins/ReoID/virus-nos-by-country.htm

The recent EFSA output on BT showed that the BTV presence has been demonstrated in different organs, including lymphoid tissue, skin and reproductive organs. The maximum duration of the presence of BTV is registered in the spleen up to 40 days for infectious virus and up to 3 months for its nucleic acid (EFSA AHAW Panel, 2017a).

In a recent paper submitted for publication (Puggioni et al., 2016), a BTV-1 infected blood sample collected from an ewe with BT clinical signs during the 2006 Sardinia outbreak and stored in the fridge at + 4°C, was able to cause clinical signs when inoculated in a ram 10 years later.

#### 3.3.1.6. Article 7(a)(vi) The routes and speed of transmission of the disease between animals, and, when relevant, between animals and humans routes of transmission

*Routes of transmission*

Parameter 1 – Types of routes of transmission from animal to animal (horizontal, vertical)

The usual route of BTV (1–24 serotypes) transmission to its animal (ruminant) hosts is via the bites of virus-infected haematophagous *Culicoides* midges that act as biological vectors of the virus (Gibbs and Greiner, 1994; Nevill, 1971; Mellor et al., 2000; Carpenter et al., 2013). Vector midges play a crucial role to the natural epidemiology and spread of BTV. Here below the main routes of transmission are described:

**Vector midges** (*Culicoides* spp.) can fly short distances of 1–2 km, but they can be blown much further by wind. Long distance spread of BTV from endemic regions to adjacent uninfected areas can occur via the wind-borne dissemination of virus-infected midges, especially over water (Sedda et al., 2012; Burgin et al., 2013). Thus, novel strains of BTV regularly are introduced by windborne midges from Indonesia to the 'Top End' of Australia, and into Mediterranean Europe from North Africa (Calistri et al., 2004a; Lorusso et al., 2013a; Eagles et al., 2014). Infected midges were likely responsible for the spread of BTV-16 from Italy to Croatia (Listeš et al., 2009), from Sardinia to Corsica (BTV-2 in 2000, BTV-4 in 2003, BTV-16 in 2004, BTV-1 in 2013) and BTV-8 from mainland Europe to the UK in 2007 (Gloster et al., 2010; Szmaragd et al., 2010). Similarly, recent incursions of novel serotypes of BTV into the south-eastern United States are perhaps the result of spread by windborne midges carrying viruses that circulate in the Caribbean Basin (Johnson, 2007; Gibbs et al., 2008; Maclachlan, 2011).

**The movement of BTV-infected animals** can be responsible for translocation of BTV, however, such occurrences are only important if the local vector population within the receiving region is able to efficiently acquire and transmit the introduced virus. For example, a novel strain of BTV-2 that recently appeared in California is closely related to viruses from Florida, suggesting this virus was translocated across the continental United States by animal movement and then spread by vectors in California (Maclachlan et al., 2013). Similarly, the spread of BTV-8 from France to Italy in 2007–2008 were likely due to movement of infected cattle (Giovannini et al., 2008), as well as the spread of BTV-14 from Poland to Spain (ref), the spread of BTV-1 from south-west France to Britanny (Defra, 2008), and the import of pregnant cattle to Ireland from the Netherlands (Menzies et al., 2008).

**Vector-independent transmission** of BTV clearly can occur, although its significance is largely unknown. The epidemiology of BTV-25, 26 and 27 infection of goats appears to be different than that of the other serotypes (BTV-1–24) and may not involve *Culicoides* midges (Vogtlin et al., 2013). In fact, BTV-25 and BTV-27 do not replicate in *Culicoides* cells and the viraemia in infected animals is longer than in BTV-1–24.

Recent studies also demonstrated **direct contact transmission** of BTV-26, likely by aerosol, between goats (Batten et al., 2014). In fact, although the kinetics of BTV-26 infection in sheep and goats are similar to those of BTV-25, the virus can be horizontally transmitted to uninfected, in-contact goats which subsequently seroconvert (Batten et al., 2013a, 2014). This indicated that unlike BTV-25, BTV-26 can be transmitted horizontally by direct contact and replicates in mammalian cells (BHK-21, BSR and Vero cells) *in vitro*, but does not replicate in KC cells.

In a study conducted in dromedaries in Mauritania slaughterhouse, BTV-26 neutralising antibodies were found in a high number of animals confirming that horizontal transmission may have occurred in this case at the slaughterhouse, where animals are gathered together for several days before slaughtering (Lorusso et al., 2016). There is also evidence that BTV-26 cannot infect at least one species of midges known to be a BTV vector (*Culicoides sonorensis*) suggesting that an alternative horizontal transmission mechanism may be essential for this virus (Pullinger et al., 2016).

BTV-27 has been observed that during an experimental infection, a control in-contact goat was infected by direct transmission (Breard et al., in preparation). In field conditions, the spread of BTV-27 seems to be limited in space, differently than the one by vector spread (Breard et al., in preparation).

**Oral BTV infection** of both ruminant livestock and wild or zoo carnivores has been described, including infection of calves via the feeding of infective colostrum (Alexander et al., 1994; Mayo et al., 2010) and experimentally via cultured viruses or urine from an experimentally infected sheep. At least some BT strains (including members of serotypes 1, 2 and 8) can be transmitted directly between ruminants in close contact (van der Sluijs et al., 2011; Rasmussen et al., 2013; van der Sluijs et al., 2013b). The mechanisms of contact transmission are still uncertain. Suggestions have included shared feed and water troughs, contamination of wounds with blood during fighting among red deer, and contact with infected placentas in a case in cattle. This is a newly recognised route, and is generally thought to be of little epidemiological significance compared to transmission by midges for the expansion of an outbreak, although the long duration of pregnancy in cattle suggests that vertical transmission and the release of virus at birth may provide an important overwintering route and may therefore be epidemiologically significant, even if relatively infrequent. Seropositive dogs, cats and wild carnivores in Africa were thought to have eaten tissues from infected animals, and Eurasian lynx in a zoo that died after infection with BTV-8 had been fed ruminant fetuses and stillborn animals from outbreak areas. However, seropositive dogs in Morocco had not been fed raw diets, suggesting that they may have been infected by *Culicoides*.

**Contamination of biological products**, notably those that utilise fetal bovine serum, is also well described as, for example, in canine and cattle vaccines (Akita et al., 1994). Primary ruminant cell lines may also be a source of contamination, such as lamb testis cells contaminated with BTV-28 (Bumbarov et al., 2016).

Vertical transmission of BTV in animals certainly does occur, notably with live attenuated vaccine strains of BTV and European BTV-8, but this route is considered unlikely to be important to the initial expansion of natural BTV outbreaks (Verwoerd and Erasmus, 2004; Maclachlan et al., 2009; Saegerman et al., 2011; van der Sluijs et al., 2014; EFSA AHAW Panel, 2017a). Some of these animals can be born infected and may allow BTV to overwinter, with the potential to introduce the virus to new areas if the dam is transported. Transplacental transmission (TPT) has been demonstrated in dogs, at least for serotype 11 (Akita et al., 1994). For BTV serotypes other than BTV-8, TPT was experimentally demonstrated for BTV-2 in sheep and BTV-11 in cattle and North American elk (EFSA AHAW Panel, 2017a).

BTV-8 has been detected in the **semen of naturally infected bulls** by both PCR and virus isolation, indicating that BTV-8 may contaminate semen in a similar way to tissue culture-passaged viruses. Further work is required to investigate the duration of the BTV-8 presence in semen. Apart from BTV-8, field/wild strains of BTV have only been identified in the semen of older bulls, most likely due to blood contamination. It has been demonstrated that females inseminated with cell-culture-adapted BTV-contaminated semen can become infected. The vast majority of evidence shows that isolation of BTV in semen coincides with the viraemic period in the bull/ram. However, one study showed that a tissue culture-passaged strain of BTV-1 was detected in semen for approximately 10 days beyond the period of detectable viraemia in the bull. In general, recipient animals have not shown evidence of infection after receiving embryos from infected donors, apart from one study with BTV-11 in which the recipient heifers sero-converted.

In some circumstances, the **human role in mediating the introduction of BTV vaccine viruses**, rather than animal movement has been suggested (De Clercq et al., 2009; Reviriego Gordejo, 2013). For example, the recent appearance of at least three (BTV-6, BTV-11 and BTV-14) different South African live-attenuated BTV vaccine strains among livestock in Europe (most recently BTV-14 in western Russia, Poland and Lithuania) has been recorded. Interestingly, live-attenuated vaccine strains of BTV-6 and BTV-11 first appeared in the same general region of northern Europe as did BTV-8 in 2006 (Enserink, 2006), again suggesting an as yet unexplained anthropogenic phenomenon. Similarly, in India, strains of BTV-2 and -10 that are genetically similar or identical to live attenuated vaccine viruses used elsewhere in the world have also been identified as infecting local livestock, raising further concerns regarding the unauthorised international movement of vaccine viruses (Maan et al., 2012a,b). Bluetongue virus can also be spread mechanically on surgical equipment and needles (Darpel et al., 2016).

*Speed of transmission*

As in the methodology opinion, transmission/transmissibility is described by two parameters, incidence and transmission rate (EFSA, 2007).

Parameter 3 – Incidence between animals and, when relevant, between animals and humans

Information on different levels of incidence for different BTV strains/serotypes is shown in Table 1, based on ADNS data since 1999. The observed incidence is very variable, even within the same serotype, but all 'historical' serotypes were categorised in the impact table as high or medium transmissibility capacity at least for one strain (with the exception of BTV-16); on the contrary, the routes of spread of goat strains are not totally clarified, thus even the speed of spread is not known but supposedly to be low.

Parameter 4 – Transmission rate (beta) (from $R_0$ and infectious period) between animals and, when relevant, between animals and humans

A large number of heterogeneities related to vectors hosts and the environment influence both spatial and temporal variation in $R_0$, for example, the distribution of ruminant and vector species, and regional differences in environmental factors, in particular, temperature (Anderson and May, 1991). Although full risk assessment needs to take these factors into account and produce spatiotemporal maps for $R_0$, transmission models often inevitably ignored them. A recent EFSA output showed that $R_0$ for BT exceed the value of 1 for temperatures ranging from 9.1 (in case of 20 *Culicoides* caught) to 11.5°C (in relation to five *Culicoides* caught), thus roughly confirming possible thresholds around 10°C for disease transmission (EFSA AHAW Panel, 2017a,b,c).

Although combining data of many serotypes for estimating some parameters (duration of host viraemia, extrinsic incubation period) there may be differences among serotypes and, in particular, interactions between host, virus and vector, which influence the ability of BTV to invade a host population. For example, BTV- 2, -9 and -16 have all been introduced to Europe, but have not extended much beyond the northern rim of the Mediterranean basin (Mellor and Wittmann, 2002; Purse et al., 2005; Lorusso et al., 2014), while BTV-8 has appeared and spread in northern Europe (Elbers et al., 2007), and BTV-1 spread right though Iberia into central France. This is showed also in the impact table (Section 3.3), according to the spread capability to other episystems, which occurs only for BTV-1, 4 and 8.

Uncertainty and sensitivity analyses based on Latin hypercube sampling and partial rank correlation coefficients identified temperature, the probability of transmission from host to vector and the vector-to-host ratio as being most important in determining the magnitude of $R_0$. The importance of temperature reflects the fact that it influences many processes involved in the transmission of BTV and, in particular, the biting rate, the extrinsic incubation period and the vector mortality rate (Gubbins et al., 2008). The risk is greatest when the temperature is between 15°C and 25°C. At lower temperatures, BTV is unable to replicate to transmissible levels, while at higher temperatures the vector is less likely to survive for long enough to complete the extrinsic incubation period. Temperature appears to be the main factor when basic reproduction numbers were applied to determine the vector seasonal period in Austria. $R_0$ above one was found between June and August except in the mountainous regions of the Alps, at altitude where the midges are absent. The highest values coincide with the locations of confirmed BTV cases (Brugger and Rubel, 2013).

Although sophisticated airborne and ecological models may be beneficial, sometimes relatively simple analyses of basic epidemiological data can be more appropriate. In Italy, for example, a quite uncomplicated risk assessment based on animal movement data allowed for identifying the areas at risk for BTV-8 virus introduction (Giovannini et al., 2008). This shows that the general approach of parsimony in the model complexity should always be followed (Calistri et al., 2013).

As reported in Table 1, there are some extreme situations, like the case of BTV-16, for which a very limited transmission rate can be considered. Despite the absence of any vaccination against this serotype and specific movement control policies, BTV-16 virus circulation was quite limited in few geographical areas of Italy. The reasons behind the limited spread of this serotype are not fully clear (Lorusso et al., 2013b).

De Koeijer et al. (2011) estimated different $R_0$ values around 4 for the second half of the summer, and falling below 1 by autumn for Germany, Belgium and the Netherlands related to the BTV-8 epidemic in 2006, confirming the effects of host and vector variables to the speed of transmission of the disease. Obviously, the speed of transmission is strongly influenced by the vector abundance and,

therefore, by the local climatic conditions. Napp et al. (2016) estimated the case-reproduction ratio ($R_t$) for the BTV-1 spread in Andalusia in 2007, resulting in values ranging from 4.6 in July, to 2.2 in August, and below 1 in September (0.8) and October (0.02).

The expected level of vector transmission of some vector-borne diseases addressed in previous EFSA output (EFSA AHAW Panel, 2017c) including BT, epizootic haemorrhagic disease virus (EHDV), Palyam virus (KASV), BTV and equine encephalosis virus (EEV) is considered high in the EU, with $R_0$ values between 3 and 10. Several factors are contributing to these high $R_0$ values, such as the long infectious periods in the host reported in experimental infections (e.g. medians of 17.5, 16.5, 21.3 and 16.5 dpi for EHDV, KASV, BTV and EEV, respectively). Further, the high numbers of the vectors per hosts estimated (average of 20 vectors per host), the high biting rate (0.51 on average) contributed to the high $R_0$ values.

#### 3.3.1.7. Article 7(a)(vii) The absence or presence and distribution of the disease in the Union, and, where the disease is not present in the Union, the risk of its introduction into the Union

*Presence and distribution*

Parameter 1 – Map where the disease is present in EU

In Figures 3 and 4, a map shows where BTV has been present in the EU in 2016–2017.

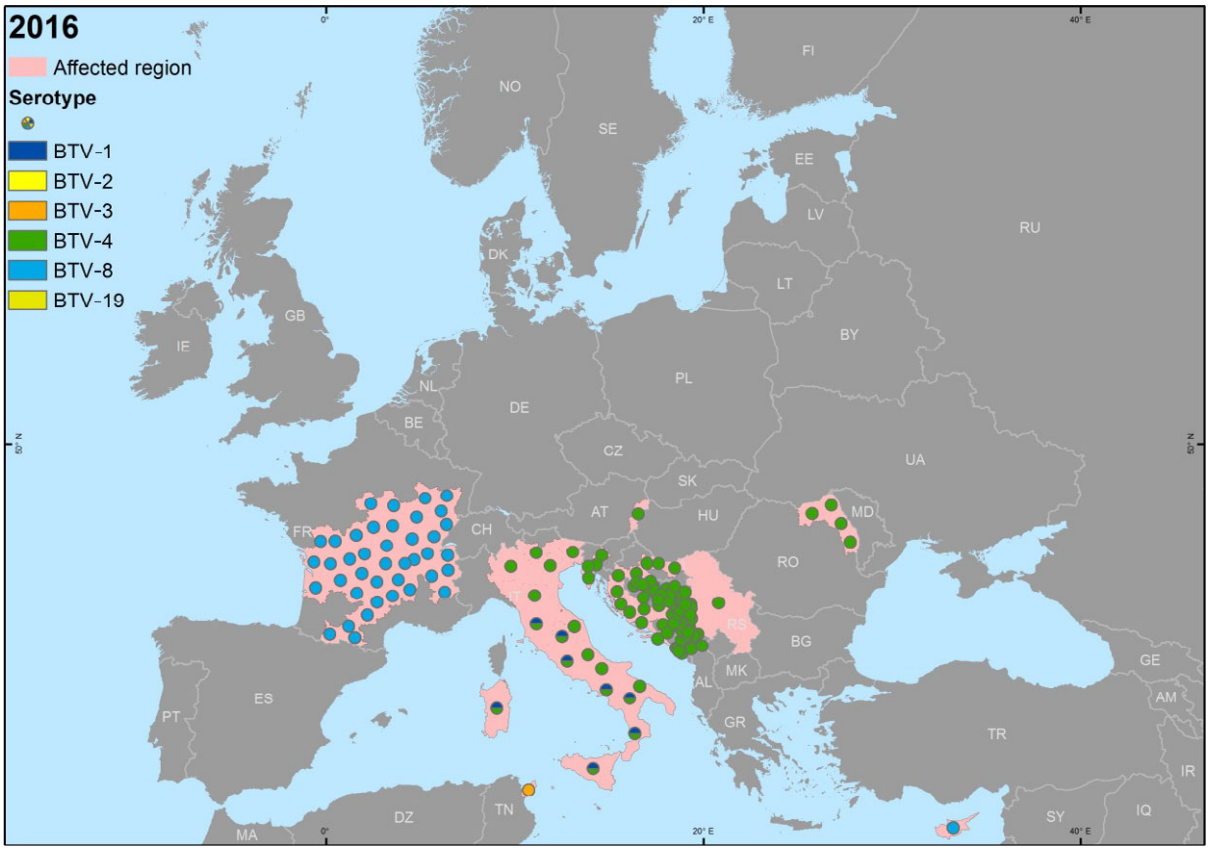


**Figure 3:** BTV serotypes reported to ADNS in the EU in 2016

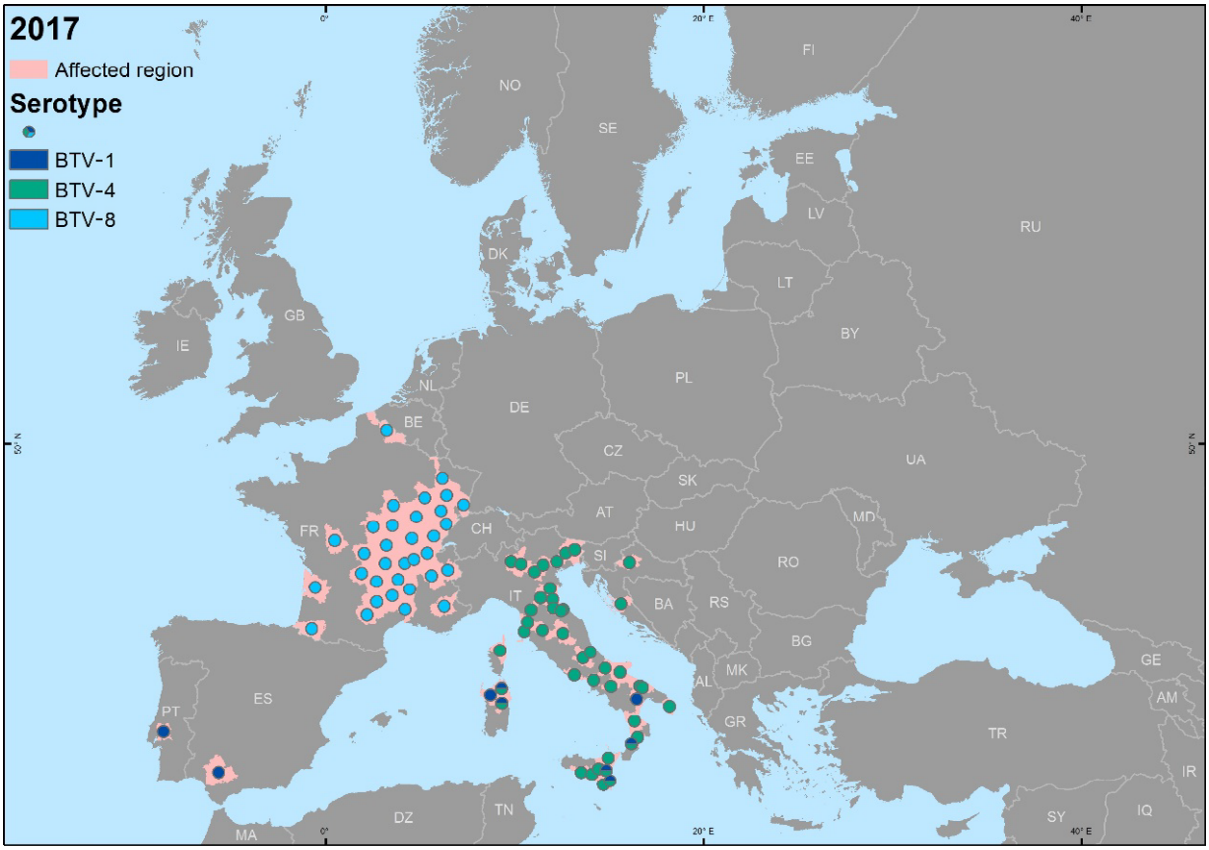


**Figure 4:** BTV serotypes currently reported to ADNS in the EU in 2017 up to April

Temporal maps for each year showing the distribution of BTV serotypes in EU since 1999 until 2015 are shown in the Annex A to the present opinion.

Parameter 2 – Type of epidemiological occurrence (sporadic, epidemic, endemic) at MS level

Traditionally, the virus was present in a geographic band between the latitudes 40°N and 35°S where its vectors, certain species of biting midges, were living (Rodrıguez-Sanchez et al., 2008; Vellema, 2008; Wilson and Mellor, 2009). In North America, Europe and China, the virus spread even further, up to 50°N (Mellor et al., 2000; Agren et al., 2010). Endemic areas exist in Africa, Europe, the Middle East, North and South America and Asia, as well as on numerous islands (e.g. Australia, the South Pacific, the Caribbean and the Mediterranean). Multiple serotypes can be found in many regions.

The recent EFSA output on BTV showed that some *Culicoides* species, in some geographical areas in Europe or during years with mild winter temperatures, i.e. are active throughout the year, thus allowing BTV overwintering, as the example of serotype 8 virus that overwintered for multiple years in central and northern Europe. However, there are periods of the year when the abundance of the *Culicoides* vector species is extremely low, mainly coinciding with winter low to very low temperatures, in particular in northern Europe. Long-standing practical experience demonstrates that transmission of BTV is substantially reduced or halted during these periods.

Historically, Europe has experienced only sporadic incursions of BT, involving a single virus serotype on each occasion (Mellor and Boorman, 1995). However, since 1998, BTV spread northwards into the Mediterranean Basin, where seven BTV serotypes (1, 2, 4, 8, 9, 16 and 27) have been identified (Purse et al., 2005). In the summer of 2006, for the first time, the BTV has crossed latitude 50°N and BT outbreaks caused by BTV-8 occurred in north-western Europe: the Netherlands, Belgium, Germany, France and Luxembourg (Wilson and Mellor, 2008). In 2007–2008, the BT situation changed for the worse, BTV-8 spread to the other regions of Europe and the number of outbreaks increased rapidly. Additionally, two new BTV serotypes, BTV-11 and BTV-6, were detected (Wilson and Mellor, 2009). A new virus, similar to BTV, and infecting goats was discovered in Switzerland in early 2008. It was named *Toggenburg orbivirus* (Hofmann et al., 2008), and is a so far unknown orbivirus with low pathogenicity and a potential BTV-25 (Hofmann et al., 2008; Chaignat et al., 2009).

BTV-2 and BTV-4 were eradicated from territories such as the Balearic Islands merely using vaccination. However, the implementation of BT compulsory vaccination programmes in Europe resulted in a massive reduction of BTV-8 cases. BTV was eradicated from central (partially) and northern Europe; however, it is still circulating in some regions of central, southern and south-eastern Europe. In 2012, BTV-4 and BTV-1 were present in Sardinia. In 2013, disease caused by BTV-1 was spreading extensively over the territory of Italy (Sardinia, Sicily and mainland Italy). At the beginning of 2014, the same BTV serotype has been isolated in Corsica (France). Moreover, BTV-1 cases were noticed in the west Spain, outbreaks caused by BTV-4 in south Spain (Andalusia) and in the region of Algarve in Portugal. In 2014, outbreaks of BTV-4 have been confirmed in Greece (Peloponnese and Evros regions). In July, the first outbreak of BTV-4 was also reported at the south Bulgaria and from there it spread to Bulgaria, Romania and all Balkan countries and southern Italy. In 2015, BTV-4 continued circulating in the Balkan Peninsula and Italy. In the same year BTV-8 re-emerged in France. The current BTV circulation in Europe is displayed in Figure 3 and 4.

Regarding the epidemiological status of MS in relation to BT, it has to be said that the status could be related to the occurrence of a single or multiple serotypes. According to the recent history of BT in Europe, it is reasonable to say that BT is endemic in the countries of southern and eastern Europe. BTV-8 is likely endemic in France. In the other countries of central and northern Europe, BT is epidemic, although it is sporadic in the countries of the Scandinavian Peninsula and the UK.

*Risk of introduction*

The disease was introduced and already circulating in the EU.

Gerbier et al. (2008) estimated, from the epidemic in the northern part of western Europe, the rate of BTV-8 spread after introduction into a naïve population at 15 km/week. However, Calistri et al. (2004b) estimated the rate for BTV-2 in Sardinia at 30 km/week. Spread of BTV-infected vectors by air across open water may even be beyond 30 km, as shown by the incursion of BTV into the UK (Gloster et al., 2010). Moreover, Ducheyne et al. (2007) reported that windborne-spread of BTV-infected vectors over sea may be possible for a distance of up to 750 km. However, spread over such a long distance across land has never been published. Hendrickx et al. (2008) estimated that, in 2006, 50% of the spread from an infected farm in Belgium took place within a 5 km radius and 95% within a 30 km radius. Using a different model, De Koeijer et al. (2011) estimated that 85% of the secondary infections of BTV-8 took place within a 15-km radius of an infected farm. However, Szmaragd et al. (2010) predicted even more localised spread than the De Koeijer et al. model. Both studies used the same outbreak data set, including comparable assumptions on data, but assuming different spatial transmission kernels (probability of infection as a function of the distance to an infectious source) during model fitting. This likely explains the detailed differences between derived spreading distances. Nevertheless, the results of both studies suggest a local to intermediate spatial transmission. Taking the information above into account (and assuming that infection starts in the centre of the grid) means that the currently defined geographical unit for monitoring and surveillance (45 $\times$ 45 km) covers spatial spread of BTV infection of a few weeks. According to Reynolds et al. (2006), local spread of BTV is mostly caused by active movements of the vectors themselves in all directions and is rather symmetric, while the medium and long distance spread is caused by windborne movement of vectors and animal movements and may follow a rather asymmetric pattern. Although increasing the size of the zone considered to be infected might give more protection to surrounding free zones, results from De Koeijer et al. (2011) suggest that doing this increases the amount of long distance spread of BTV within the zone considered to be infected.

### 3.3.1.8. Article 7(a)(viii) The existence of diagnostic and disease control tools

*Diagnostic tools*

Parameter 1 – Existence of diagnostic tools

Virus detection

Various techniques have been used to detect the presence of the virus, antigen or viral RNA. The most commonly used were: real time RT-PCR, conventional RT-PCR on agarose gel, capture enzyme-linked immunosorbent assay (ELISA), viral isolation from embryonated chicken eggs and viral isolation from mammal or insect cells. Traditional RT-PCR and real-time RT-PCR assays provide a versatile system able to give information on orbivirus serogroup and serotype within a few hours. They are also highly sensitive and capable of detecting very low concentrations of viral RNA. In addition, real-time

assays are able to quantify the viral genome. Due to all these advantages, in most laboratories, these new techniques are preferred to classical viral detection and identification techniques, which require three to four weeks to be completed. However, RT-PCRs are actually not able to distinguish whether the RNA detected in the animal is part of an infectious virus or just RNA of degraded or neutralised virus that is no longer able to infect the vector. The classical virus isolation technique (inoculation of embryonated chicken eggs/mammal cells or insect cells/mammal cells), or transmission to another naive host are still the only methods able to reveal the presence of infectious virus in an animal. Several studies have confirmed that, at least for some BTV serotypes, RNA could be detected in the blood longer than infectious virus (MacLachlan et al., 1994; Singer et al., 2001; Bonneau et al., 2002; Di Gialleonardo et al., 2011). The sensitivity of the RT-PCR in determining BTV circulation is dependent on the duration of viral RNA persistence in the blood of the host. Based on the detection of BTV RNA in cattle for months following infection (Bonneau et al., 2002; Di Gialleonardo et al., 2011), real-time RT-PCR could be considered a valid and sensitive method for determining BTV circulation in cattle.

Both the live and inactivated vaccines recently deployed in Europe generate an immune response to all of the BTV proteins. It has not therefore been possible to develop an effective serological assay to distinguish infected from vaccinated animals (DIVA). The real-time PCR assay does not detect inactivated vaccines for significant periods post-inoculation, and has therefore been used as a DIVA assay to allow continued surveillance during recent vaccination campaigns in Europe.

Antibody detection

Several techniques can be used to detect the presence of BTV-specific humoral antibodies in animals which have either been infected with BTV or vaccinated against the virus. The methods enabling the detection of BTV serogroup-specific antibodies in the serum and milk of infected animals most commonly used are: competitive ELISA (c-ELISA), milk ELISA and for detection of serotype specific antibodies, micromethod plate seroneutralisation (SN). The OIE has prescribed the competitive ELISA (c-ELISA) serological test for bluetongue diagnosis for international trade. Over time, the accuracy of this assay has been progressively improved through the use of antigens obtained from recombinant structural proteins of BTV. The competitive ELISA, using direct antibodies against the VP7 protein that is common to all BTV serotypes, detects the presence of antibodies to all 27 BTV serotypes. The technique is highly sensitive and specific, with its specificity being due to the use of a monoclonal antibody specific for VP7, the protein that distinguishes the BT serogroup from other *Orbivirus* species/serogroups. It is able to determine the presence of antibodies no matter which serotype the BTV strain belongs to, and represents the preferred method to determine and monitor BTV circulation, since it is cheap, sensitive and specific. However, in cases where the population is vaccinated, it cannot be used to identify infections, unless unvaccinated sentinels are tested as well. Although some kits have been developed (see, for example, Barros et al., 2009), no serological DIVA tests for discriminating BTV-infected from vaccinated animals are at the moment commercially available.

Milk ELISAs have also been developed that successfully assess the antibody status of animals with respect to BTV infection. The advantage of these tests is that they can be used on bulk milk samples, which has the obvious benefit of testing groups of animals in one step, avoiding the need for blood sampling (Kramps et al., 2007). Its specificity was recently improved by precipitating the milk protein prior to carrying out the ELISA (Chaignat et al., 2009). However, once vaccines have been used a persistent positive signal from vaccinated animals may reduce the value of these assays for surveillance.

As ELISAs are not able to distinguish between BTV serotypes, in areas where more than one serotype has been circulating, the serum neutralisation assay is needed to determine the prevalence of each BTV serotype. Serum neutralisation (SN) is the only serological method so far able to determine the viral serotype responsible for the infection (serotype-specific test). Serotype identification is feasible by RT-PCR.

*Control tools*

Control of BT is attempted using either preventive (prophylactic) or therapeutic strategies (Verwoerd and Erasmus, 2004; Papadopoulas et al., 2009; Maclachlan and Mayo, 2013; Zientara and Sanchez-Vizcaino, 2013). Treatment of BT-affected ruminants is often unrewarding and logistically challenging during outbreaks as it involves only nonspecific supportive and nursing care. Prevention of BT and/or BTV infection of ungulates can be achieved either by protecting animals from insect attack or prophylactic immunisation (vaccination). Elimination of *Culicoides* midges from the environment is not practical generally, particularly in extensive pastoral settings. However, housing animals in protected buildings during the peak of activity (dusk, early evening) to minimise exposure to biting

midges can be beneficial for vector species that exhibit strictly outdoor (exophagy) feeding behaviour, but less so with those species that exhibit indoor (endophagy) feeding behaviour. Especially valuable animals can be housed in vector-protected establishments to prevent any contact with vector midges with 96% of efficacy (EFSA AHAW Panel, 2017a) during outbreaks, or treated with repellents to minimise the likelihood of vector attack. Vaccination is central to prevention of BT in many endemic areas, and also to the response to incursions of the disease into previously unaffected regions (Verwoerd and Erasmus, 2004; Savini et al., 2008). Zientara et al., 2010; McVey and Maclachlan, 2015).

### 3.3.2. Article 7(b) The impact of diseases

#### 3.3.2.1. Article 7(b)(i) The impact of the disease on agricultural and aquaculture production and other parts of the economy

*The level of presence of the disease in the Union*

Parameter 1 – Number of MSs where the disease is present

As shown in Section 3.3.1.7, the MSs where BTV is currently present are France, Italy, Spain, Portugal, Croatia (Figures 3 and 4).

*The loss of production due to the disease*

Parameter 2 – Proportion of production losses (%) by epidemic/endemic situation

Losses due to any livestock disease may be classified as losses in production (direct losses), expenditure and lost revenue (indirect losses) (Rushton, 2009). In case of BT in Europe, most studies on the estimation of direct losses on production due to the disease impact are related to the epidemic of BTV-8 occurrence in 2006–2008 in northern Europe. For the other serotypes, an estimation of the direct losses can be derived by the morbidity and mortality rates (see Table 1). The impact of BT in endemic situations appears to be relatively small and is dominated by the impacts on flock and herd fertility as well as vaccination. There are issues with regard the adoption of improved breeds and there is evidence that where new and more productive breeds are incorporated into livestock systems BT becomes more important. In this situation, the major costs is linked to the management of animal vaccination for control and prevention of the disease (see Section 3.3.5).

In epidemic situations, the impacts are much more diffuse. First, there are naïve populations of animals and the possibility of deaths of older more valuable animals is relevant. Fertility issues also cause problems, particularly in systems where even small losses in calf, lamb or kid production can affect the economic viability of a system. There are also well reported losses of milk production. However, the largest and most serious impact with BT in epidemic situations is related to the reactions to the presence and risk of the disease. Significant resources are spent on new vaccines, and serious restrictions are placed on animal movements. There are also impacts on markets. In short, the reaction to the disease is usually large and perhaps in hindsight far greater than the production losses usually caused by the disease itself. More details have been given in Section 3.3.5. In the epidemic situation, the net costs depend on the virulence of the strain responsible of the incursion. It could be much higher, as for the BTV-8 epidemic of 2006–2008, but also irrelevant as for the incursion of BTV-11 or BTV-6. Most information is available for BTV-8 epidemic in 2006–2009 in northern Europe. For BTV-8 in the Netherlands, the cost of the 2006 epidemic was estimated at 32.4 million euros. The net costs of the BTV-8 epidemic of 2007 (BT2007) was valued at 164–175 million euros, depending on the mortality and morbidity rates for cattle used. The losses accounted for 2%, 10% and 11% of the gross value of the primary production within Dutch pasture-based livestock farming that equalled 1.6 billion euros. Control measures accounted for 91% of the net costs of the BTV-8 2006, while diagnostic costs represented 7%. By contrast, for the BTV-8 2007, 92% of the net costs was in the form of production losses and veterinary treatment fees, while only 6% were related to control measures (Velthuis et al., 2010).

Velthuis et al. (2010) constructed a deterministic economic model to determine the cost of the BTV-8 epidemic in the Netherlands during 2006 and 2007. Cattle, sheep and goat sectors were incorporated and the model considered the impact of production, treatment of diseased animals, diagnostic, and control measure costs. The criteria to assess the impact on production included mortality, early culling, decreased milk production, weight loss, no gestations, post-poned gestations, abortions, still births, decreased fertility of rams and lower birth weights (Table 5). All parameters were based on expert opinion of private and government veterinarians, who were involved in the epidemic.

**Table 5:** The considered parameters for assessing the production impact in cattle, sheep, and goat sectors used in the analysis of the BTV-8 economic impact in the Netherlands provided by Velthuis et al. (2010). 2006: estimate from July 2006 to July 2007. 2007: estimate from July 2007 to July 2008

| Parameter | Cattle | | Sheep | | Goats | |
|---|---|---|---|---|---|---|
| | 2006 | 2007 | 2006 | 2007 | 2006 | 2007 |
| Early culling (%) | 3 | 3 | 3 | 0 | 0 | 0 |
| Weight loss (%) | 7.0 | 7.0 | 8.1 | 8.1 | – | – |
| No gestation (%) | 5.2 | 9.9 | 5.0 | 9.8 | – | – |
| Postponed gestation (%) | 36.9 | 53.5 | 0.0 | 10.0 | – | – |
| Abortion (%) | 2.0 | 6.2 | 1.9 | 3.2 | – | – |
| Reduced fertility rams (%)[a] | – | – | 0.0 | 75.0 | – | – |
| Reduced birth weight (%) | 2.6 | 6.7 | – | – | – | – |
| Stillbirths (%) | 0.0 | $5.3 \times 10^{-4}$ | – | – | – | – |
| Average daily milk production (kg/day) | 26.9 | 26.9 | 2.0 | 2.0 | | 2.48 |
| Relative reduction milk production (%) | 20 | 20 | 20 | 20 | – | 80 |

(a): Percentage of sheep farms that needed 1 extra ram.

### Milk yield losses

Two studies attempted to use empirical data to quantify the reduction in milk yield due to BTV-8 on immunologically naïve herds. A prospective study in the Netherlands monitored 15 seronegative herds (1,074 cows) for seroconversion from July to December 2008 (Santman-Berends et al. 2011a). The authors found that seroconverted cows produced 52 kg (95% CI 26–76) less milk (between 0.3% and 0.9% less) of the annual production. No effect on somatic cell count was detected. A study from France quantified the mean impact on milk yield at the farm level and the duration of reduction before and after the date disease was detected accounting for the risk of exposure at a district level (Nusinovici et al., 2013). Over 3,000 Holstein herds were included in the study and the herds acted as their own controls by comparing data from the same herd preoutbreak with what was subsequently produced after BTV exposure. This study found that comparing the exposed and unexposed periods in high-exposure areas, the mean cumulative loss was 3.4% of the annual 305-day production. This period of reduction was between 2 months before to 4 months after the reported date of disease detection in the herd.

### Fertility losses

Several studies attempted to quantify the impact of BTV on fertility. Saegerman et al. (2011) investigated an outbreak on a 355-ewe sheep flock in Belgium of which around 60% had clinical disease from July to September 2007. Data from four subsequent lambing periods were also presented (November 2007, January 2008, March 2008 and May 2008). A higher rate of abortions of 15.7% was detected in the lambing period in 2008; the rate was higher when compared to the rate of earlier periods, which ranges between 0% and 5.7%. The authors also found that the fertility rate (number of pregnant ewes/number of ewes used) had decreased down to 30% from the 59–76% recorded in earlier periods (Saegerman et al., 2011).

Regarding cattle, Santman-Berends et al. (2010) monitored fertility on the 15 seronegative Dutch herds. They found that infected cows were 5 times (95% CI 1.9–14.3) more likely to return to service (RTS) within 56 days after first insemination and were 1.7 times less likely (95% CI 1.4–2.0) to become pregnant compared to non-infected cows.

On French dairy farms, Nusinovici et al. (2012) looked at the effect of BTV-8 on the 90 day RTS rate after first insemination, revealing an increased rate of between 8% and 21% comparing exposed and non-exposed herds, depending on the time interval between the date of insemination and the date of detection in the herd. In cantons of high exposure, this effect was estimated at between 13.5% and 26.8%. In a different study, the same authors also looked at the rate of late RTS between 90 and 200 days and short gestations. The authors reported an average effect of BTV-8 exposure with a 6.7% increase in RTS and 1.9% increase in short gestations when exposed from the third month of gestation inwards (Nusinovici et al., 2012). In Israel, BTV infection has not been associated with fertility problems in cattle (Shimshony, 2004).

#### 3.3.2.2. Article 7(b)(ii) The impact of the disease on human health

Humans are not susceptible to BTV and therefore there is no direct impact on public health.

#### 3.3.2.3. Article 7(b)(iii) The impact of the disease on animal welfare

Parameter 1 – Severity of clinical signs at case level and related level and duration of impairment

The severity of clinical forms of BT for the 'historical serotypes' and the goat strains can be observed from the impact table and deduced by the measure of morbidity, mortality and case fatality reported in Table 1. In general for all 'historical serotypes', with the possible exception of BTV-16, the clinical form of the disease are variable but can be severe, while for the serotypes BTV-25, -27, -30, it is asymptomatic.

After infection by insect bite, the virus replicates first in the adjacent lymph node and then spreads to infect vascular endothelium and macrophages/dendritic cells in many tissues/organs. Virus-induced injury to endothelial cells in small blood vessels leads to vascular thrombosis and ischemic necrosis of the tissues involved (DeMaula et al., 2002), which may induce lesions such as acute oral ulceration, coronitis, muscle necrosis and vascular leakage leading to facial and pulmonary oedema as well as pleural and pericardial effusion. These clinical conditions may lead to poor welfare in the animals to a considerable degree, causing pain and malaise. Euthanasia is appropriate for animals with severe muscle necrosis or severe coronitis, as these are unlikely to make a full recovery (Dercksen and Lewis, 2007). For these reasons, in several Member States legislation recognises and advocates the euthanasia for the animals in these clinical conditions providing for farmer compensation.

#### 3.3.2.4. Article 7(b)(iv) The impact of the disease on biodiversity and the environment

*Biodiversity*

Parameter 1 – Endangered wild species affected: listed species as in CITES and/or IUCN list

The following wild animal species can be affected by the BTV serotypes from 1 to 24.
Species least concerned:

- Musk ox, *Ovibos moschatus*, Bovidae, Artiodactyla
- Alpine ibex, *Capra ibex*, Bovidae, Artiodactyla
- Siberian ibex, *Capra sibirica*, Bovidae, Artiodactyla
- Giraffe, *Giraffa camelopardalis*, Giraffidae, Artiodactyla
- Collared peccary, *Pecari tajacu*, Tayassuidae, Artiodactyla
- Eurasian lynx, *Lynx lynx*, Felidae, Carnivora
- Spotted hyena, *Crocuta crocuta*, Canidae, Carnivora
- Jackal, *Canis mesomelas*, Canidae, Carnivora
- Large spotted genet (*Genetta tigrina*), Viverridae, Carnivora
- White-tailed deer, *Odocoileus virginianus*, Cervidae, Artiodactyla
- Red deer, *Cervus elaphus*, Cervidae, Artiodactyla (Howerth et al., 2001; Fernandez-Pacheco et al., 2008; Ruiz-Fons et al., 2008; Rodriquez-Sanchez et al., 2010)
- Wapiti elk, *Cervus canadensis*, Cervidae, Artiodactyla; (Howerth et al., 2001; Fernandez-Pacheco et al., 2008; Ruiz-Fons et al., 2008; Rodriquez-Sanchez et al., 2010)
- Roe deer, *Capreolus capreolus*, Cervidae, Artiodactyla (Howerth et al., 2001; Fernandez-Pacheco et al., 2008; Ruiz-Fons et al., 2008; Rodriquez-Sanchez et al., 2010)
- Axis deer, *Axis axis*, Cervidae, Artiodactyla; (Howerth et al., 2001; Fernandez-Pacheco et al., 2008; Ruiz-Fons et al., 2008; Rodriquez-Sanchez et al., 2010)
- Fallow deer, *Dama dama*, Cervidae, Artiodactyla; (Howerth et al., 2001; Fernandez-Pacheco et al., 2008; Ruiz-Fons et al., 2008; Rodriquez-Sanchez et al., 2010)
- Sika deer, *Cervus nippon*, Cervidae, Artiodactyla; (Howerth et al., 2001; Fernandez-Pacheco et al., 2008; Ruiz-Fons et al., 2008; Rodriquez-Sanchez et al., 2010)
- Moose, *Alces alces*, Cervidae, Artiodactyla
- Reeve's muntjac, *Muntiacus reevesi*, Cervidae, Artiodactyla
- Bighorn sheep, *Ovis canadensis*, Bovidae, Artiodactyla (Fernandez-Pacheco et al., 2008)
- Blue wildebeest, *Connochaetes taurinus*, Bovidae, Artiodactyla
- Black wildebeest, *Connochaetes gnou*, Bovidae, Artiodactyla
- Buffalo, *Syncerus caffer*, Bovidae, Artiodactyla (Tessaro and Clavijo, 2001; Niedbalski, 2015)
- Red hartebeest, *Alcelaphus buselaphus*, Bovidae, Artiodactyla
- Spanish ibex, *Capra pyrenaica*, Bovidae, Artiodactyla

- Springbok, *Antidorcas marsupialis*, Bovidae, Artiodactyla
- Pronghorn, *Antilocapra americana*, Bovidae, Artiodactyla, (Tessaro and Clavijo, 2001; Niedbalski, 2015)

Among the vulnerable species:

- Musk deer, *Moschus moschiferus*, Cervidae, Artiodactyla; (Howerth et al., 2001; Fernandez-Pacheco et al., 2008; Ruiz-Fons et al., 2008; Rodriquez-Sanchez et al., 2010)
- Mouflon, *Ovis orientalis,* Bovidae, Artiodactyla (Fernandez-Pacheco et al., 2008)
- Arabian oryx, *Arabian oryx,* Bovidae, Artiodactyla
- Nubian ibex, *Capra nubiana,* Bovidae, Artiodactyla
- African elephant, *Loxodonta africana*, Elephantidae, Proboscidea
- Cheetah, *Acinonyx jubatus*, Felidae, Carnivora
- Lions, *Panthera leo*, Felidae, Carnivora
- European bison/wisents, *Bison bonasus*, Bovidae, Artiodactyla

Among the near threatened species:

- American bison, *Bison bison,* Bovidae, Artiodactyla (Tessaro and Clavijo, 2001; Niedbalski, 2015)
- White rhinoceros, *Ceratotherium simum,* Rhinocerotidae, Perissodactyla
- Blackbuck, *Antilope cervicapra*, Bovidae, Artiodactyla

Among the endangered species:

- African wild dogs, *Lycaon pictus,* Canidae, Carnivora

Among the critically endangered species:

- Wild bactrian camel, *Camelus ferus*, Camelidae, Artiodactyla
- Addax, *Addax nasomaculatus*, Bovidae, Artiodactyla
- Black rhinoceros, *Diceros bicornis,* Rhinocerotidae, Perissodactyla

Parameter 2 – Mortality in wild species

Data on mortality in wild animals have been described in Section 3.3.1.2 about case-fatality rate.

*Environment*

Parameter 3 – Capacity of the pathogen to persist in the environment and cause mortality in wildlife

BTV, as a virus, can persist in the environment only inside the host and/or the vector. As mentioned before, the virus could stay viable for many months and sometimes years in tissue and blood samples stored refrigerated, or at −70°C. Apart from the viraemic host, vector midges play an important role in maintaining the virus in the environment. They may play a role in the interseasonal maintenance of BTV in temperate regions, so-called virus overwintering (Nevill, 1971; Wilson et al., 2008). The percentage of *Culicoides* midges that become infected after taking a BTV-infected blood meal from an animal host can vary with virus strain, *Culicoides* species/population and environmental factors, particularly temperature. The infected midges can become infectious after an incubation period of approximately 10 days (depending on ambient temperature), which is required for the virus to disseminate from the gut to the salivary glands of the vector (Mullens et al., 1995; Mellor, 2000). Once infected with BTV, female midges remain persistently infected for the remainder of their lives. Although the average life span of these is usually ten to 20 days (Mellor, 2000), they can occasionally live for up to 3 months (Lysyk and Danyk, 2007). As explained above (Section 3.3.1.5) under favourable conditions, some biting midges can live long enough to survive the period between two vector seasons (EFSA AHAW Panel, 2017a).

### 3.3.3. Article 7(c) Its potential to generate a crisis situation and its potential use in bioterrorism

*Potential to generate crisis situation*

BTV is among the pathogens that may generate high consequences for livestock industry and trade, linked to direct and indirect losses, in particular at first incursion in naive populations There are example of crises generated I Sardinia (Italy) and Spain when BTV entered in naive small ruminant populations.

*Potential use in bioterrorism*

BTV is not included in the list of potential bioterrorist agents, neither for human nor for animal diseases, neither in the list of the Encyclopaedia of Bioterrorism Defense of Australia Group or any other list of potential bioagroterrorism agents.

### 3.3.4. Article 7(d) The feasibility, availability and effectiveness of the following disease prevention and control measures

#### 3.3.4.1. Article 7(d)(i) Diagnostic tools and capacities

*Availability*

Parameter 1 – Officially/internationally recognised diagnostic tool, OIE certified

The diagnostic methods for bluetongue and their purpose are indicated in the OIE Manual of Diagnostic Tests and Vaccines for Terrestrial Animals (2017),[6] as reported in Table 6.

**Table 6:** Test methods available for the diagnosis of bluetongue and their purpose

| Method | Purpose | | | | | |
|---|---|---|---|---|---|---|
| | **Population freedom from infection** | **Individual animal freedom from infection prior to movement** | **Contribute to eradication policies** | **Confirmation of clinical cases** | **Prevalence of infection – surveillance** | **Immune status in individual animals or populations post-vaccination** |
| **Agent identification**[(a)] | | | | | | |
| **Real-time RT-PCR** | – | +++ | – | +++ | ++ | – |
| **RT-PCR** | – | +++ | – | +++ | ++ | – |
| **Classical virus isolation** | – | +++ | – | +++ | – | – |
| **Detection of immune response** | | | | | | |
| **c-ELISA (serogroup specific)** | ++ | +++ | ++ | – | ++ | ++ |
| **VN (serotype specific)** | ++ | +++ | ++ | – | ++ | ++ |
| **AGID** | + | – | + | – | + | + |
| **CFT** | + | – | + | – | + | + |

Key: +++ = recommended method; ++ = suitable method; + = may be used in some situations, but cost, reliability, or other factors severely limits its application; – = not appropriate for this purpose.
Although not all of the tests listed as category +++ or ++ have undergone formal validation, their routine nature and the fact that they have been used widely without dubious results, makes them acceptable.
RT-PCR = reverse-transcription polymerase chain reaction; c-ELISA = competitive enzyme-linked immunosorbent assay; VN = virus neutralisation; AGID = agar gel immunodiffusion; CFT = complement fixation test.
(a): A combination of agent identification methods applied on the same clinical sample is recommended.

*Effectiveness*

Parameter 2 – Se and Sp of diagnostic test

See also Section 3.3.1.8.

Serological diagnosis of previous BTV infection of livestock is usually now done by c-ELISA that detects antibodies to the BTV VP7 core protein (Afshar, 1994). When properly validated, the test is highly sensitive and specific, and detects antibodies to most if not all serotypes and strains of BTV. Antibodies detected by c-ELISA persist for long periods following BTV infection of animals, although c-ELISA does not distinguish animals that were naturally infected with BTV from those that were

[6] http://www.oie.int/fileadmin/Home/eng/Health_standards/tahm/2.01.03_BLUETONGUE.pdf

immunised with current live-attenuated BTV vaccines (DIVA). It is to be stressed that the presence of BTV-specific antibody by c-ELISA indicates only prior exposure to BTV and implies nothing about disease causality or when that infection occurred. Serotype specific antibody is assessed using virus-serum neutralisation assay in cell cultures, a procedure that takes several days and requires specialised laboratory facilities to complete.

Identification of BTV infection in animals is most readily accomplished using a group-specific quantitative PCR (RT-qPCR) assay. Such assays now are routinely available in many diagnostic laboratories, and at least one of these assays (based on detection of the S10 gene that encodes NS3 (Hofmann et al., 2008) has consistently identified all field strains of BTV to date, regardless of serotype and region of origin (genetic topotype). A distinct advantage of RT-qPCR over conventional PCR assays is that the amount of viral nucleic acid in a sample can be quantitated, which can be useful in ascribing disease causality; specifically, acutely affected animals generally have large amounts of BTV nucleic acid in their blood and tissues, which is reflected by low Ct values on the RT-qPCR assay.

Critically, ruminants remain positive for BTV nucleic acid by PCR assay for up to 6 months or longer following infection, meaning that the mere detection of viral nucleic acid by RT-qPCR is not proof of the presence of infectious virus (Maclachlan et al., 1994; Bonneau et al., 2002; Maclachlan et al., 2009; OIE, 2013a). Unlike conventional RT-PCR assays, the real-time RT-PCR assays can be used in a 'closed- tube' format, reducing the risk of contaminating the working laboratory environment with amplified DNA, and therefore reducing the risks of false positive results. Serotype-specific PCR assays can be used to type the virus present in samples that are positive by group-specific assay (Maan et al., 2012a,b; Mayo et al., 2012). The availability of these assays has largely obviated the need for virus isolation as part of diagnostic testing and 'typing', which is complex, laborious, expensive and typically takes several weeks to perform. Hence, virus isolation requires specialised laboratory facilities. Furthermore, some virus strains require initial propagation in embryonated chicken eggs before they will grow in cell culture systems. However, virus isolation does demonstrate conclusively that the viral RNA detected by RT-PCR is present in infectious virus particles, not just as RNA or DNA copies of the viral genes.

Quantitative assessment of the diagnostic sensitivity and specificity of tests used in the EU monitoring and surveillance programmes is important to allow the establishment of the predictive values of positive and negative results for a given prevalence. Vandenbussche et al. (2008) reported a diagnostic sensitivity and specificity for the real time RT-PCR of 99.5% (95% CI: 99.0–100) and 98.5% (97.1–100), respectively. Based on these figures, this test is good for using during monitoring and surveillance in phases 2–4, however, when testing large numbers of negative animals (phase 1 or 5) some false positive test results may be observed. Specificity can be increased if positive results are subsequently tested by a serotype specific PCR. Moreover, the epidemiological situation can be taken into account in case of unforeseen positive results. Consequently, PCR is a good test for the purpose of monitoring and surveillance. However, standardisation of this assay between different countries and laboratories is required.

The outcomes of the most up-to-date systematic review on the sensitivity and specificity of c-ELISA are provided in Table 7.

**Table 7:** Summary outcomes of systematic review on the sensitivity and specificity of diagnostic tools used to detect BTV infections (papers published up to January 2016)

| Diagnostic tool type | Species | Sensitivity range (%) | Specificity range (%) |
|---|---|---|---|
| **Competitive ELISA (c-ELISA)** | Cattle | 89.2 (83.0–100) | 98.4 (95.8–99.5) |
| | Sheep | 83.8 (12.8–91.1) | 95.5 (69.5–99.8) |
| | Goats | 92.8 | 94.8 |

Regarding the performances of milk ELISAs, they depend on the herd prevalence. Mars et al. (2010) reported a herd sensitivity of 88% (95% CI 80–94) at a within-herd prevalence of 1%, accompanied by a specificity of 100% (95% CI 96–100), and a herd sensitivity of 100% (95% CI 96–100) at a within-herd prevalence of 10%, accompanied by a specificity of 93% (86–98).

*Feasibility*

Parameter 3 – Type of sample matrix to be tested (blood, tissue, etc.)

- Midges
- Live animals: blood in EDTA

- Freshly dead animals: spleen, lymph nodes, red bone marrow, heart blood
- Aborted and congenitally infected newborn animals: spleen, brain, lymph nodes
- All samples have to be preserved at 4°C, and not frozen (−20°C)
- Paired sample sera

See also Section 3.3.1.8.

#### 3.3.4.2. Article 7(d)(ii) Vaccination

*Availability*

Parameter 1 – Types of vaccines available on the market (live, inactivated, DIVA, etc.)

The first generation of commercial bluetongue vaccines was live attenuated vaccines (LAVs). For the largest part of the 20th century, use of these vaccines was restricted to southern Africa and North America, and intended to limit clinical disease. South African vaccines contain in total 15 serotypes divided in three pentavalent vaccines subsequently injected with intervals of 3–4 weeks, resulting in broad cross-protection against the multiplicity of BTV serotypes endemic to the region (Dungu et al., 2004).

In North America, similar LAVs for prevailing serotypes were developed and used in sheep and captive cervids since the 1950s. Autogenous, inactivated vaccines are also available. They are custom-made vaccines that contain herd specific (homologous) antigens. They usually contain combinations of BTV and EHDV antigens. Little published data are available for the evaluation of these products (McVey and Maclachlan, 2015).

In the late 1990s, the BTV incursion in southern Europe led briefly to the use of South African LAV in Italy, Corsica and Spain (Zientara and Sanchez-Vizcaino, 2013, Pérez de Diego et al., 2011). Safety considerations led to the development of safer, inactivated vaccines, against the serotypes relevant to the European outbreak situation. The first commercial BT vaccine of the second generation (i.e. inactivated vaccines) was introduced by Merial in Italy in 2003, under Temporary Authorisation of Use (Savini et al., 2008). Several European manufacturers introduced other inactivated vaccines in Europe under the same regulatory framework: temporary authorisations of use, conditional licences or registrations under exceptional circumstances. These temporary authorisations were later converted into full marketing authorisations (Saegerman et al., 2007; Savini et al., 2008)

Registration in the EU follows the strict regulatory guidelines set by the European Pharmacopeia and the EMA Committee for Medicinal Products for Veterinary Use (CVMP). Production must follow European Good Manufacturing Practices (EU-GMP).

LAVs were used in India until 2015 followed by the introduction of inactivated vaccines (Ranjan et al., 2015). An inactivated pentavalent vaccine is in current use in India.

In China, inactivated vaccines have been produced and used in several provinces in response to outbreaks (Zhang et al., 2004), but little information on these products is available and they do not seem to be part of regular vaccination programs.

Vaccines of the third generation (recombinant and engineered vaccines) have proven to be safe and effective at the experimental scale, and have the potential to address some of the weaknesses of inactivated vaccines, like DIVA capability, rapid onset of immunity and cross-serotype protection. However, development and registration of a new vaccine represents a major R&D investment, and would be justified financially for a manufacturer only by a significant advantage over existing inactivated vaccines. As of 2017, none has been registered and made available commercially. Vaccines by country of registration are listed in Table 8.

**Table 8:** Vaccines by country of registration

| Company | Product Name | Serotype | Vaccine type* | Adjuvant | License countries | Indications |
|---|---|---|---|---|---|---|
| **Vaccines licensed for use in the EU** | | | | | | |
| Bioveta | BioBos BTV8 | 8 | I | Aluminium hydroxide, Saponin | Czech Republic | Cattle, Sheep |
| CZ Veterinaria | BLUEVAC BTV8 | 8 | I | Aluminium hydroxide, Saponin | EU | Cattle, Sheep |

| Company | Product Name | Serotype | Vaccine type* | Adjuvant | License countries | Indications |
|---|---|---|---|---|---|---|
| CZ Veterinaria | BLUEVAC-1 | 1 | I | Aluminium hydroxide, Saponin | Spain, France | Cattle, Sheep |
| CZ Veterinaria | BLUEVAC-4 | 4 | I | Aluminium hydroxide, Saponin | Spain | Cattle, Sheep |
| Merial | BTVPUR AlSap | 1, 8, 2, 4 + any combination of 2 of these strains** | I | Aluminium hydroxide, Saponin | EU | Cattle, Sheep |
| Merial | BTVPUR AlSap 9 | 9 | I | Aluminium hydroxide, Saponin | Italy | Cattle, Sheep |
| MSD Animal Health | Bovilis BTV-8 | 8 | I | Aluminium hydroxide, Saponin | EU | Cattle, Sheep |
| Syva | Syvazul-1 | 1 | I | Aluminium hydroxide, Saponin | EU | Cattle, Sheep |
| Syva | Syvazul-1+8 | 1, 8 | I | Aluminium hydroxide, Saponin | Spain | Cattle, Sheep |
| Syva | Syvazul-4 | 4 | I | Aluminium hydroxide, Saponin | Spain | Sheep |
| Syva | Syvazul-8 | 8 | I | Aluminium hydroxide, Saponin | Spain | Cattle, Sheep |
| Zoetis | ZULVAC 1 + 8 Ovis | 1+8 | I | Aluminium hydroxide, Saponin | EU | Sheep |
| Zoetis | ZULVAC 8 Ovis | 8 | I | Aluminium hydroxide, Saponin | EU | Sheep |
| Zoetis | ZULVAC 8 Ovis | 8 | I | Aluminium hydroxide, Saponin | EU | Cattle |
| Zoetis | ZULVAC 1 Ovis | 1 | I | Aluminium hydroxide, Saponin | EU | Sheep |
| Zoetis | ZULVAC 1 Bovis | 1 | I | Aluminium hydroxide, Saponin | EU | Cattle |
| Zoetis | ZULVAC 1 + 8 Bovis | 1+8 | I | Aluminium hydroxide, Saponin | EU | Cattle |
| Zoetis | Zulvac 4 Ovis | 4 | I | Aluminium hydroxide, Saponin | Spain | Sheep |
| **Vaccines licensed for use in India** | | | | | | |
| Biovet Private Limited | BioBT-Oil | 1+2+10+16+ 23 | I | Oil | India | Sheep and Goats |
| Biovet Private Limited | BioBT-Gel | 1+2+10+16+ 23 | I | Aluminium hydroxide, Saponin | India | Sheep and Goats |

| Company | Product Name | Serotype | Vaccine type* | Adjuvant | License countries | Indications |
|---|---|---|---|---|---|---|
| Indian Imunologicals | Raksha Blu | 1+2+10+16+ 23 | I | Aluminium hydroxide, Saponin | India | Sheep and Goats |
| **Vaccines licensed for use in China PR** | | | | | | |
| Yunnan Tropical and Subtropical Animal Virus Disease Laboratory | Bluetongue vaccine | 1+16 | LAV<br>I | ? | China PR | Sheep and Goats |
| **Vaccines licensed for use in Morocco** | | | | | | |
| Biopharma | BTVAC | 1+4 | LAV | | Morocco | Sheep and Goats |
| MCI Santé Animale | OVIVAX BT1+4 | 1+4 | LAV | | Morocco | Sheep and Goats |
| **Vaccines licensed for use in Russia** | | | | | | |
| National Research Institute for Veterinary Virology and Microbiology of Russia | Bluetongue Vaccine | 1,6,8,4,9,16 | I | Aluminium hydroxide, Saponin | Russia | Sheep and Goats |
| **Vaccines licensed for use in South Africa** | | | | | | |
| Onderstepoort Biological Products | Bluetongue Vaccine For Sheep | A: 1+4+6+12+14<br>B:3+8+9+10+11<br>C:2+5+7+13+19 * | LAV | | South Africa | Sheep |
| **Vaccines licensed for use in Turkey** | | | | | | |
| Etlik Veterinary Control Central Research Institute | Blue-T4 ETVAC Mavi Dil Asisi | 4 | LAV | | Turkey | Sheep |
| **Vaccines licensed for use in the USA** | | | | | | |
| Colorado Serum Company | Bluetongue Vaccine | 10 | LAV | | USA | Sheep and Goats |
| Newport Laboratories | Custom made EHD+BTV Vaccine | Autogenous EHD + BTV, serotypes on demand (EHD1+2 +6 BTV17+3) | I, CM | Oil | USA | Cervids only |
| Poultry Health Laboratories (PHL) | BlueVac | 10, 11, 17 | LAV | | California | Sheep |

*: I = inactivated; LAV = Modified Live Virus; CM = Custom-Made (autogenous).
**: BTVPUR was registered under the multistrain guideline that allows combinations of strains suited to the epidemiology.

*Effectiveness*

Parameter 3 – Field protection as reduced morbidity (as reduced susceptibility to infection and/or to disease)

Data about protection conferred by BT vaccine are shown in Table 9.

**Table 9:** Detailed references and values from a systematic review on the efficacy of BTV vaccines approved for commercialisation in the European Union (papers published up to January 2016)

| | Vaccine commercial name (BTV serotype) | Doses | Species | Efficacy | Prevention of clinical signs |
|---|---|---|---|---|---|
| Breard et al. (2015) | **BTVPUR ALSAP 8** | 1 | Sheep | Full protection against BTV serotype 8 in challenge 21 days after vaccination (no viraemia, demonstrated immunogenicity) | Clinical scores summed over 2 weeks after challenge were 7 times smaller than controls |
| Breard et al. (2015) | **BTVPUR ALSAP 2,4** | 2 | Sheep | Poor protection against BTV serotype 8 (viraemia and clinical signs detected after challenge, no neutralising antibodies on the day of challenge) | Clinical scores summed over 2 weeks after challenge were not significantly lower than controls |
| Gubbins et al. (2012) | **Bovilis BTV8** | 2 | Cattle | Efficacy calculated based on number of infections prevented (proportional reduction) = 75% (CI: 60–85) | |
| Gubbins et al. (2012) | **Bovilis BTV8** | 1 | Sheep | Efficacy calculated based on number of infections prevented (proportional reduction) = 98% (CI: 89–100) | |
| Moulin et al. (2012) | **Bovilis BTV8** | 1 | Sheep (young animals) | High protection against BTV serotype 8 in challenge 21 days after vaccination (1/16 animals showing viraemia, demonstrated immunogenicity) | Clinical scores summed over 2 weeks after challenge were 8–10 times smaller than controls |
| Moulin et al. (2012) | **Bovilis BTV8** | 1 | Sheep (adults) | High protection against BTV serotype 8 in challenge 21 days after vaccination (2/12 animals showing viraemia, demonstrated immunogenicity) | Clinical scores summed over 2 weeks after challenge were 4–7 times smaller than controls |
| Breard et al. (2011) | **Bovilis BTV8** | 2 | Goats | Full protection against BTV serotype 8 in challenge 21 days after vaccination (no viraemia, demonstrated immunogenicity) | Not reported |
| Breard et al. (2011) | **BTVPUR ALSAP 8** | 2 | Goats | Full protection against BTV serotype 8 in challenge 21 days after vaccination (no viraemia, demonstrated immunogenicity) | Not reported |

Parameter 4 – Duration of protection

LAVs confer lifelong protection as with natural infection. For inactivated vaccines, producers recommend annual booster, thus immunity is supposed not to be longer than 12 months.

For inactivated vaccine of BTV-2 and 4, two doses fully protect sheep for up to 12 months, while in cattle although a single dose of BTV-4 inactivated vaccine prevented viraemia in vaccinated animals challenged 2 weeks after vaccination, a single vaccination did not fully prevent viraemia in animals challenged 7 months after vaccination (Savini et al., 2008). For the inactivated BTV serotype 8, the duration of immunity is not yet fully established in cattle or sheep, although interim results of ongoing studies demonstrate that the duration is at least 6 months after the primary vaccination course in sheep.[7]

*Feasibility*

Parameter 5 – Way of administration

Live-attenuated BT vaccines are administered subcutaneously whereas inactivated BT vaccines may be administered by subcutaneous or intradermal injection. Currently used live-attenuated or inactivated BTV vaccines have reported protective immunity upon challenge between 7 and 12 months and yearly revaccination is often conservatively adopted in the field (Savini et al., 2004b; Hamers et al., 2009a,b; Oura et al., 2009; Waeckerlin et al., 2010). Booster vaccination increased the antibody responses

[7] http://www.merial.co.uk/Livestock/Pages/bluetongue.aspx

compared to single vaccinations, and, especially in cattle, repeated vaccination and a high dose is considered necessary for long-lasting protection (Hund et al., 2012). Surprisingly, however, anti-BTV antibodies including neutralising antibodies have been reported for up to 4 years in ruminants following the BTV-8 vaccination campaign using different inactivated preparations (Eschbaumer et al., 2012; Oura et al., 2012; Batten et al., 2013b). Although protection was not confirmed in challenge experiments, vaccination with inactivated vaccines may potentially protect ruminants for longer periods than initially assumed.

#### 3.3.4.3. Article 7(d)(iii) Medical treatments

No specific treatment is available, other than supportive care. Symptomatic treatment and care includes non-steroidal anti-inflammatory drugs (NSAID) to reduce pain, fluid therapy to treat or prevent dehydration, provision of shade against the sun, protection against extremes of temperature, use of mild disinfectants to irrigate affected areas, general nursing care, the provision of a trough of cool water in which affected animals can cool their muzzle, provision of soft green foods during the period when the mouth lesions are painful, and long-acting antibiotics against secondary bacterial diseases. For animals with severe coronitis or severe muscle necrosis, euthanasia is appropriate (Dercksen and Lewis, 2007; Kaandorp-Huber, 2008).

Cattle are more likely to recover more quickly than are sheep. Affected sheep should be housed to protect them from direct sunlight and from extreme temperatures and offered soft green foods while the mouth lesions are painful (Veterinary Research Laboratory Onderstepoort, 1963). If necessary, fluids and electrolytes could be given. It may be necessary to control secondary infections. Mild disinfectants may be used to irrigate affected areas; this may provide some relief for affected animals. (Radostits et al., 2007).

#### 3.3.4.4. Article 7(d)(iv) Biosecurity measures

Since bluetongue (serotypes BTV-1–24) is considered to be non-contagious by direct contact, isolation of infected animals is not necessary or appropriate for disease control. Other measures could be adopted in order to reduce the contact between hosts and vectors.

Recently, the effectiveness of vector-control measures has been reviewed in an EFSA opinion (EFSA AHAW Panel, 2017a), and compared to the effectiveness of vector-proof establishments. It was concluded that there is no conclusive evidence that the use of insecticides or repellents when applied singularly reduce the transmission of BTV in the field. In specific scenarios, however, they have been shown to either kill *Culicoides* or reduce host/vector contact and hence are used as a risk mitigation measure where vaccines are unavailable.

Housing of livestock during the times when the vector midges are most active, i.e. dusk to dawn, should significantly reduce rates of biting by exophilic vectors (Osburn, 2000; Mellor and Wittmann, 2002). The effectiveness of stabling or protective housing is likely to vary considerably depending on the *Culicoides* species involved as well as how "midge-proof" the housing is (Carpenter et al., 2008a,b).

Screens applied on openings (windows, doors) using fine mesh capable of excluding midges, or coarser mesh impregnated with a suitable insecticide such as a synthetic pyrethroid should further reduce the attack rate (EFSA AHAW Panel, 2017a).

Treatment of animals with pour-on insecticides causes mortality in a proportion of feeding *Culicoides*; thus, preventing further onward transmission from a host that is infected and viraemic, thereby helping to stop further spread of the outbreak. However, the effect is transient and necessitates frequent application. Furthermore, high level of efficacy (up to 86%) of pour-on insecticides is difficult to achieve, particularly under field conditions, and little information is available about the effect of reduction on the numbers of engorged *Culicoides* females in relation to BTV transmission (EFSA AHAW Panel, 2017a). Repellents that act prior to feeding may be more likely to prevent *Culicoides* feeding and could therefore prevent the initial infection of a susceptible and naïve animal. Nevertheless treatment of animals with repellent products (e.g. diethyl toluamide (DEET)) has been less investigated, largely due to the logistics of reapplication every few hours. This is unlikely to be feasible except for very high value stock (EFSA AHAW Panel, 2017a).

#### 3.3.4.5. Article 7(d)(v) Restrictions on the movement of animals and products, as control measure

The movement control of animals and biological products can limit the spread of BTV infection between different regions and countries. However, in the restricted areas or where the virus circulates the movement control alone cannot prevent the spread of infection by vectors.

The strict control of animal movements is one of the key factors for the control of BT spread, especially when coupled with the vaccination of susceptible animals in infected areas and the implementation of surveillance activities able to monitor the BTV circulation and to assess the risk of disease spread (Caporale and Giovannini, 2010). From 2000 to 2006 the above mentioned approach was applied in southern Europe countries like Italy, Spain and Portugal, allowing at limiting the spread of the infection northward, although the complete eradication of the infection was achieved only in few limited cases (Caporale and Giovannini, 2010).

The legal basis for the movement restrictions is laid down in Council Directive 2000/75/EC and Commission Regulation (EC) No 1266/2007. Further information is provided on the dedicated webpage of DG SANTE.[8]

#### 3.3.4.6. Article 7(d)(vi) Killing of animals

As a vector-borne disease stamping out is unlikely to have much effect and therefore there is no justification for it in case of bluetongue. This is partly because the virus is considered likely to be already present in the vector population, and the infected midges would be unaffected by removal of infected host animals. In a few cases, however, some animals may need to be euthanised for welfare reasons.

#### 3.3.4.7. Article 7(d)(vii) Disposal of carcasses and other relevant animal by-products

Among the routes of transmission, it has been described that BTV can be transmitted via oral route for example to carnivores (Section 3.3.1.6). Even though this may be a rare event, the correct disposal of infected carcases can prevent this occurrence.

### 3.3.5. Article 7(e) The impact of disease prevention and control measures

#### 3.3.5.1. Article 7(e)(i) The direct and indirect costs for the affected sectors and the economy as a whole

Detailed studies on evaluation of costs are available only for BTV-8 epidemics in 2006–2009. These may include:

- cost of control (e.g. treatment/vaccine, biosecurity)
- cost of eradication (culling, compensation)
- cost of surveillance and monitoring
- trade loss (bans, embargoes, sanctions) by animal product
- importance of the disease for the affected sector (% loss or euros lost compared to business amount of the sector)

Bluetongue is often said to be a disease with potential economic consequence qualifying it as a notifiable disease by the OIE. A global estimate of the impact of BT was US$3 billion (Bath, 1989). Southern regions of the US are endemic for some types of foot and mouth disease (FMD), which restricts trade of livestock and related products. This indirect cost has been estimated at US $125 million annually (Tabachnick, 1996). With regard to the BTV-8 outbreaks, Wilson and Mellor (2009) stated that the 'BTV-8 epidemic in northern Europe has probably caused greater economic damage than any previous single-serotype Bluetongue outbreak'.

In epidemic situations, e.g. BTV-8 epidemic in northern Europe, in 2007, the overall estimates on the financial impact in France and the Netherlands were US$1.4 billion and US$85 million, respectively. The costs are largely ascribed to the trade restrictions that were present during the outbreak period. A study commissioned by the Scottish Government led to the development of a model to estimate the economic impact of different incursion scenarios and the benefit-cost ratio of various control scenarios. The assessment of the impact on production was based on expert opinion. The direct costs, which incorporated reduced milk production, weight loss, mortality, veterinary treatments, and animal testing, were estimated at £30 million per year.

In the economic model developed by Velthuis et al. (2010) to determine the cost of the BTV-8 epidemic in the Netherlands during 2006 and 2007, the overall cost was estimated to be €32.4 and €164–175 million in 2006 and 2007, respectively. The authors estimated that control measures made up 91% of the cost in 2006. In 2007, due to the relaxation of control measures and the greater number of farms affected production losses and veterinary treatment fees made up 92% of the total

[8] https://ec.europa.eu/food/animals/animal/diseases/control-measures/bluetongue_en

costs. In response to uncertainty over the availability of vaccines, the same model was used to assess the relative benefits of different vaccine strategies for controlling a BTV-8 epidemic in 2008 (Velthuis et al., 2011). While, the production losses were the same as those estimated in 2007 with the original model, although the mortality, morbidity, and number of infected farms varied in the two scenarios. The overall financial impact (including production losses, diagnostics, treatment, and control measures) ranged from €40.9 to €41.3 million, with most losses being estimated to occur on sheep breeding farms, dairy export firms, and dairy firms (€12.6, €12.6 and €11.3 million, respectively). The highest impact was ascribed to production losses at 52.8% and 55.2% of the total net costs for the two scenarios under consideration.

As part of an evaluation of the surveillance and control program in Switzerland, Häsler et al. (2012) used a stochastic economic model to compare hypothesised baseline strategies with the interventions actually employed as part of retrospective (2008–2009) and prospective (2010–2012) analyses. In the retrospective baseline scenario, the mean estimated disease costs in 2008 and 2009 were €12.2 million and €3.6 million, respectively. In the 2011 and 2012 prospective baseline scenarios, the mean costs ranged between €2.6 million and €6.6 million per year, depending on the scenario being considered. As with the other studies, production losses were based mainly on expert opinion. The authors remarked that 'one major limitation of the present model was the lack of reliable data to estimate total disease costs'.

Movement restriction policy (MRP) was also the major cause of economic losses during BTV-8 2006–2007 BTV-8 outbreaks. In 2007, BTV outbreaks in France were estimated to cost $1.4 billion (Tabachnick et al., 2008). The French cattle industry accounts for 20% and 33% of the European dairy and suckling cows, respectively. Most of the 4 million suckling calves are born in winter and spring, and 1.4 million animals (mainly males) are sold yearly as beef weaned calves (BWC) around 6–9 month sold (more than 1,000 million euros of value). Most (66%) are sent abroad (Loirette-Baldit, 2008), with others sold to fattening units in France. Exports are defined here as BWC sold and sent out of France, either within or outside the EU. For these calving systems, MRP has a huge impact: timing for selling is crucial to fulfil contracts with fattening barns abroad, and farms have some limited stocking capacity, in particular during winter. In the French 2006, BTV-8 outbreak, farmers experienced a 21% decrease in animals sold due to the MRP (Tago et al., 2014).

Costs are also due to the surveillance programmes put in place for early detection of possible BTV introduction. The total net cost of the BTV-8 surveillance and vaccination programmes in Austria arising from the outbreak amounted to 22.8 million euro (0.86% of the national agricultural Gross Value Added), of which 32% was allocated to surveillance and 68% to the vaccination programme (Pinior et al., 2015).

Gunn et al. (2008) developed an economic model to identify, measure and value disease costs for various scenarios of BT introduction and spread in Scotland and to evaluate disease mitigation strategies. Baseline costs of surveillance and prevention were estimated to be £141 million over a 5-year time horizon and it was found that the benefits of avoiding disease incursion exceeded the costs of surveillance and prevention. Economic evaluation indicated control option 4 was likely to yield the greatest economic benefit. Direct costs (approx. £30 million per annum) were much smaller than indirect costs (loss of markets, price effects etc.). Although indirect costs are difficult to estimate, our results suggested that they may exceed £70 million per annum, reinforcing the importance of investment in baseline costs that reduces risk and limits incursions.

In endemic situation, especially in the southern hemisphere, it is clinically difficult, particularly in cattle, to detect and report new cases in passive surveillance systems, because the occurrence of BT may not be considered clinically significant to farmers. However, in this particular situation, one of the direct measurable economic impacts of BT on a local scale is the cost and the management of animal vaccination for control and prevention of the disease. Vaccination measures associated with preventive local economic factors of BT generally have a high economic impact and are complicated in some circumstances by the multiple serotypes associated with these diseases. Multiple inoculations per season are required. In southern African countries, the multivalent Onderstepoort Biological Products vaccine is widely used (Dungu et al., 2004). This vaccine is given in three doses consisting of 15 serotypes of attenuated BTV field strains. The economic impact based on vaccine sales in South Africa amounts to approximately US$2 million per year for a vaccination coverage of approximately 25% of the population (Grewar, 2016). This creates challenges in maintaining vaccine coverage and compliance, where applicable. In the majority of southern African regions, endemic BT may not be considered clinically significant to farmers, because they are more familiar with the disease. This might lead to an underestimation of the costs of the disease, especially when considering that in dairy

farming BT can significantly influence production (Barnard et al., 1998). The situation in the southern European countries where BT is endemic is slightly different. Vaccination campaigns are based on the use of inactivated vaccines and the costs are even higher. A dose of inactivated vaccine is around 0.8–1 euro for monovalent vaccine dose and 1.2 euro for a bivalent vaccine dose. In addition most of inactivated vaccines require a booster dose 3–4 weeks after the first injection and then yearly booster dose.

#### 3.3.5.2. Article 7(e)(ii) The societal acceptance of disease prevention and control measures

Not applicable.

#### 3.3.5.3. Article 7(e)(iii) The welfare of affected subpopulations of kept and wild animals

Parameter 1 – Welfare impact of control measures on domestic animals

Not applicable.

Parameter 2 – Wildlife depopulation as control measure

Not applicable.

#### 3.3.5.4. Article 7(e)(iv) The environment and biodiversity

*Environment*

Parameter 1 – Use and potential residuals of biocides or medical drugs in environmental compartments (soil, water, feed, manure)

In theory, vector control of *Culicoides* both larvae and adults appears as a potentially useful method to reduce BTV transmission in scenarios when vaccine for a particular serotype is not available, there are several serotypes circulating, the serotype/strain is low pathogenic and/or movement restrictions and protection of animals from vector bites are the only way to reduce transmission. Vector control could be also appropriate under emergency outbreak situations or where vaccines are not economically affordable (Harrup et al., 2015; Purse et al., 2015). In practice, the control of *Culicoides* and its impact on virus transmission at farm level is still poorly implemented and in most of the cases impractical from an environmental and technical point of view. The general classification of control methods are considered in (i) mechanical, (ii) chemical, (iii) biological, (iv) genetic and (v) biotechnological, and are reviewed in detail in a recent EFSA output (EFSA AHAW Panel, 2017a).

Concerning a possible environmental impact of insecticides for BTV control, in the same EFSA opinion, it has been concluded that there is no evidence on treatment of the environment with insecticides to kill either adult or larval *Culicoides* and it is unlikely to be effective due to the ubiquitous nature of *Culicoides* larval development sites in Europe. The high costs of other chemical treatments for BT vector control like pour-on insecticides or repellent products applied on animals do not allow large scale use of these products, thus unlikely to lead to an environmental damage.

*Biodiversity*

Parameter 2 – Mortality in wild species

See Section 3.3.2.4.

## 3.4. Assessment according to Article 5 criteria

This section presents the results of the expert judgement on the criteria of Article 5 of the AHL (Table 10) according to the strata of BT strains grouped as in Section 3.2:

- BTV strains belonging to serotypes BTV-1, -2, -4, -8, -9, that have circulated or are still circulating in some parts of Europe (defined from now on as BTV-1–24).
- Some strains of serotypes BTV-16 still circulating in some parts of Europe (defined from now on as BTV-16).
- Small ruminant-adapted strains, BTV strains belonging to serotypes BTV-25, -27, -30 and related isolates (defined from now on as BTV-25–30).

The expert judgement was based on Individual and Collective Behavioural Aggregation (ICBA) approach described in detail in the opinion on the methodology (EFSA AHAW Panel, 2017b). Experts

have been provided with information of the disease fact-sheet mapped into Article 5 criteria (see supporting information, Annex B), based on that the experts indicate their Y/N or 'na' judgement on each criterion of Article 5, and the reasoning supporting their judgement.

The minimum number of judges in the judgement was 10. The expert judgement was conducted as described in the methodological opinion (EFSA AHAW Panel, 2017b). For details on the interpretation of the questions, see Appendix B of the methodological opinion (EFSA AHAW Panel, 2017b).

**Table 10:** Outcome of the expert judgement on the Article 5 criteria for bluetongue

| **Criteria to be met by the disease:** According to AHL, a disease shall be included in the list referred to in point (b) of paragraph 1 of Article 5 if it has been assessed in accordance with Article 7 and meets all of the following criteria | | **Final outcome** | | |
|---|---|---|---|---|
| | | **BTV-1–24** | **BTV-25–30** | **BTV-16** |
| A(i) | The disease is transmissible | Y | | |
| A(ii) | Animal species are either susceptible to the disease or vectors and reservoirs thereof exist in the Union | Y | | |
| A(iii) | The disease causes negative effects on animal health or poses a risk to public health due to its zoonotic character | Y | N | |
| A(iv) | Diagnostic tools are available for the disease | Y | | |
| A(v) | Risk-mitigating measures and, where relevant, surveillance of the disease are effective and proportionate to the risks posed by the disease in the Union | Y | na* | Y |
| **At least one criterion to be met by the disease:** In addition to the criteria set out above at points A(i)–A(v), the disease needs to fulfil at least one of the following criteria | | | | |
| B(i) | The disease causes or could cause significant negative effects in the Union on animal health, or poses or could pose a significant risk to public health due to its zoonotic character | Y | N | |
| B(ii) | The disease agent has developed resistance to treatments and poses a significant danger to public and/or animal health in the Union | na | | |
| B(iii) | The disease causes or could cause a significant negative economic impact affecting agriculture or aquaculture production in the Union | Y | N | |
| B(iv) | The disease has the potential to generate a crisis or the disease agent could be used for the purpose of bioterrorism | Y | N | |
| B(v) | The disease has or could have a significant negative impact on the environment, including biodiversity, of the Union | N | | |

Colour code: green = consensus (Yes/No); red = not applicable (na), i.e. insufficient evidence or not relevant to judge

*: These strains have never been controlled; control measures might not be justified, since their impact is minimal. Therefore, although control measures may be proportionate, it is not possible to assess the effectiveness of risk-mitigating measures.

### 3.4.1. Outcome of the assessment on bluetongue according to criteria of Article 5(3) of the AHL on its eligibility to be listed

As from the legal text of the AHL, a disease is considered eligible to be listed as laid down in Article 5 if it fulfils all criteria of the first set from A(i) to A(v) and at least one of the second set of criteria from B(i) to B(v). According to the assessment methodology (EFSA AHAW Panel, 2017b), a criterion is considered fulfilled when the outcome is 'Yes'. According to the results shown in Table 10, BTV-1–24 complies with all criteria of the first set and with three criteria of the second set, therefore they are considered eligible to be listed as laid down in Article 5 of the AHL. BTV-25–30 and BTV-16 do not comply with criterion A(iii), therefore they are not considered eligible to be listed as laid down in Article 5 of the AHL.

## 3.5. Assessment according to Article 9 criteria

This section presents the results of the expert judgement on the criteria of Annex IV referring to categories as in Article 9 of the AHL about bluetongue (Tables 11, 12, 13, 14 and 15). The expert judgement was based on Individual and Collective Behavioural Aggregation (ICBA) approach described in detail in the opinion on the methodology. Experts have been provided with information of the disease fact-sheet mapped into Article 9 criteria (see supporting information, Annex B), based on that

the experts indicate their Y/N or 'na' judgement on each criterion of Article 9, and the reasoning supporting their judgement.

The minimum number of judges in the judgement was 9. The expert judgement was conducted as described in the methodological opinion (EFSA AHAW Panel, 2017b). For details on the interpretation of the questions see Appendix B of the methodological opinion (EFSA AHAW Panel, 2017b).

**Table 11:** Outcome of the expert judgement related to the criteria of Section 1 of Annex IV (category A of Article 9) for bluetongue

| **Criteria to be met by the disease:** The disease needs to fulfil all of the following criteria | | **Final outcome** | | |
|---|---|---|---|---|
| | | **BTV-1–24** | **BTV-25–30** | **BTV-16** |
| 1 | The disease is not present in the territory of the Union OR present only in exceptional cases (irregular introductions) OR present only in a very limited part of the territory of the Union | N | NC | N |
| 2.1 | The disease is highly transmissible | NC | | |
| 2.2 | There be possibilities of airborne or waterborne or vector-borne spread | Y | na | Y |
| 2.3 | The disease affects multiple species of kept and wild animals OR single species of kept animals of economic importance | Y | | |
| 2.4 | The disease may result in high morbidity and significant mortality rates | Y* | N | |
| **At least one criterion to be met by the disease:** In addition to the criteria set out above at points 1–2.4, the disease needs to fulfil at least one of the following criteria | | | | |
| 3 | The disease has a zoonotic potential with significant consequences on public health, including epidemic or pandemic potential OR possible significant threats to food safety | N | | |
| 4 (CI) | The disease has a significant impact on the economy of the Union, causing substantial costs, mainly related to its direct impact on the health and productivity of animals | Y | N | |
| 4 (PI) | The disease has a significant impact on the economy of the Union, causing substantial costs, mainly related to its direct impact on the health and productivity of animals | Y | N | |
| 5(a)(CI) | The disease has a significant impact on society, with in particular an impact on labour markets | N | | |
| 5(a)(PI) | The disease has a significant impact on society, with in particular an impact on labour markets | Y | N | |
| 5(b)(CI) | The disease has a significant impact on animal welfare, by causing suffering of large numbers of animals | Y | N | |
| 5(b)(PI) | The disease has a significant impact on animal welfare, by causing suffering of large numbers of animals | Y | N | |
| 5(c)(CI) | The disease has a significant impact on the environment, due to the direct impact of the disease OR due to the measures taken to control it | N | | |
| 5(c)(PI) | The disease has a significant impact on the environment, due to the direct impact of the disease OR due to the measures taken to control it | N | | |
| 5(d)(CI) | The disease has a significant impact on a long-term effect on biodiversity or the protection of endangered species or breeds, including the possible disappearance or long-term damage to those species or breeds | N | | |
| 5(d)(PI) | The disease has a significant impact on a long-term effect on biodiversity or the protection of endangered species or breeds, including the possible disappearance or long-term damage to those species or breeds | N | | |

Colour code: green = consensus (Yes/No); yellow = no consensus (NC); red = not applicable (na), i.e. insufficient evidence or not relevant to judge.

*: According to the interpretation of this criterion as described in the methodology opinion, which considers the potential of the disease to have high morbidity and/or high mortality, the potential morbidity and mortality levels have been assessed considering possible values in all susceptible animals, despite the low levels of morbidity and mortality usually observed in cattle.

**Table 12:** Outcome of the expert judgement related to the criteria of Section 2 of Annex IV (category B of Article 9) for bluetongue

| | **Criteria to be met by the disease:** The disease needs to fulfil all of the following criteria | **Final outcome** | | |
|---|---|---|---|---|
| | | **BTV-1–24** | **BTV-25–30** | **BTV-16** |
| 1 | The disease is present in the whole OR part of the Union territory with an endemic character AND (at the same time) several Member States or zones of the Union are free of the disease | Y | NC | Y |
| 2.1 | The disease is moderately to highly transmissible | Y | | N |
| 2.2 | There be possibilities of airborne or waterborne or vector-borne spread | Y | na | Y |
| 2.3 | The disease affects single or multiple species | Y | | |
| 2.4 | The disease may result in high morbidity with in general low mortality | Y* | N | |
| | **At least one criterion to be met by the disease:** In addition to the criteria set out above at points 1–2.4, the disease needs to fulfil at least one of the following criteria | | | |
| 3 | The disease has a zoonotic potential with significant consequences on public health, including epidemic potential OR possible significant threats to food safety | N | | |
| 4 (CI) | The disease has a significant impact on the economy of the Union, causing substantial costs, mainly related to its direct impact on the health and productivity of animals | Y | N | |
| 4 (PI) | The disease has a significant impact on the economy of the Union, causing substantial costs, mainly related to its direct impact on the health and productivity of animals | Y | N | |
| 5(a)(CI) | The disease has a significant impact on society, with in particular an impact on labour markets | N | | |
| 5(a)(PI) | The disease has a significant impact on society, with in particular an impact on labour markets | Y | N | |
| 5(b) (CI) | The disease has a significant impact on animal welfare, by causing suffering of large numbers of animals | Y | N | |
| 5(b)(PI) | The disease has a significant impact on animal welfare, by causing suffering of large numbers of animals | Y | N | |
| 5(c)(CI) | The disease has a significant impact on the environment, due to the direct impact of the disease OR due to the measures taken to control it | N | | |
| 5(c)(PI) | The disease has a significant impact on the environment, due to the direct impact of the disease OR due to the measures taken to control it | N | | |
| 5(d) (CI) | The disease has a significant impact on a long-term effect on biodiversity or the protection of endangered species or breeds, including the possible disappearance or long-term damage to those species or breeds | N | | |
| 5(d)(PI) | The disease has a significant impact on a long-term effect on biodiversity or the protection of endangered species or breeds, including the possible disappearance or long-term damage to those species or breeds | N | | |

Colour code: green = consensus (Yes/No); yellow = no consensus (NC); red = not applicable (na), i.e. insufficient evidence or not relevant to judge.

*: According to the interpretation of this criterion as described in the methodology opinion, which considers the potential of the disease to have high morbidity and/or high mortality even in absence of control measures, the potential morbidity and mortality levels have been assessed considering possible values in all susceptible animals, despite the low levels of morbidity and mortality usually observed in cattle.

**Table 13:** Outcome of the expert judgement related to the criteria of Section 3 of Annex IV (category C of Article 9) for bluetongue

| **Criteria to be met by the disease:** The disease needs to fulfil all of the following criteria | | **Final outcome** | | |
|---|---|---|---|---|
| | | **BTV-1–24** | **BTV-25–30** | **BTV-16** |
| 1 | The disease is present in the whole OR part of the Union territory with an endemic character | Y | N | Y |
| 2.1 | The disease is moderately to highly transmissible | Y | | N |
| 2.2 | The disease is transmitted mainly by direct or indirect transmission | Y | | |
| 2.3 | The disease affects single or multiple species | Y | | |
| 2.4 | The disease usually does not result in high morbidity and has negligible or no mortality AND often the most observed effect of the disease is production loss | N | N | |
| **At least one criterion to be met by the disease:** In addition to the criteria set out above at points 1–2.4, the disease needs to fulfil at least one of the following criteria | | | | |
| 3 | The disease has a zoonotic potential with significant consequences on public health, or possible significant threats to food safety | N | | |
| 4(CI) | The disease has a significant impact on the economy of parts of the Union, mainly related to its direct impact on certain types of animal production systems | N | | |
| 4(PI) | The disease has a significant impact on the economy of parts of the Union, mainly related to its direct impact on certain types of animal production systems | N | | |
| 5(a)(CI) | The disease has a significant impact on society, with in particular an impact on labour markets | N | | |
| 5(a)(PI) | The disease has a significant impact on society, with in particular an impact on labour markets | Y | N | |
| 5(b)(CI) | The disease has a significant impact on animal welfare, by causing suffering of large numbers of animals | Y | N | |
| 5(b)(PI) | The disease has a significant impact on animal welfare, by causing suffering of large numbers of animals | Y | N | |
| 5(c)(CI) | The disease has a significant impact on the environment, due to the direct impact of the disease OR due to the measures taken to control it | N | | |
| 5(c)(PI) | The disease has a significant impact on the environment, due to the direct impact of the disease OR due to the measures taken to control it | N | | |
| 5(d)(CI) | The disease has a significant impact on a long-term effect on biodiversity or the protection of endangered species or breeds, including the possible disappearance or long-term damage to those species or breeds | N | | |
| 5(d)(PI) | The disease has a significant impact on a long-term effect on biodiversity or the protection of endangered species or breeds, including the possible disappearance or long-term damage to those species or breeds | N | | |

Colour code: green = consensus (Yes/No).

**Table 14:** Outcome of the expert judgement related to the criteria of Section 4 of Annex IV (category D of Article 9) for bluetongue

| **Criteria to be met by the disease:** The disease needs to fulfil all of the following criteria | | **Final outcome** | | |
|---|---|---|---|---|
| | | **BTV-1–24** | **BTV-25–30** | **BTV-16** |
| D | The risk posed by the disease in question can be effectively and proportionately mitigated by measures concerning movements of animals and products in order to prevent or limit its occurrence and spread | NC | na | NC |
| The disease fulfils criteria of Sections 1, 2, 3 or 5 of Annex IV of AHL | | Y | N | N |

Colour code: green = consensus (Yes/No); yellow = no consensus (NC); red = not applicable (na), i.e. insufficient evidence or not relevant to judge.

**Table 15:** Outcome of the expert judgement related to the criteria of Section 5 of Annex IV (category E of Article 9) for bluetongue

| Diseases in category **E need to fulfil criteria of Sections 1, 2 or 3 of Annex IV of AHL** and/or the following: | | Final outcome | | |
|---|---|---|---|---|
| | | **BTV-1–24** | **BTV-25–30** | **BTV-16** |
| E | Surveillance of the disease is necessary for reasons relating to animal health, animal welfare, human health, the economy, society or the environment (If a disease fulfils the criteria as in Article 5, thus being eligible to be listed, consequently category E would apply.) | Y | N | N |

Colour code: green = consensus (Yes/No).

### 3.5.1. Non-consensus questions

This section displays the assessment related to each criterion of Annex IV referring to the categories of Article 9 of the AHL where no consensus was achieved in form of tables (Tables 16, 17 and 18). The proportion of Y, N or `na' answers are reported, followed by the list of different supporting views for each answer.

**Table 16:** Outcome of the expert judgement related to criterion 1 of Article 9 for BTV-25–30

| **Question** | | **Final outcome** | **Response** | | |
|---|---|---|---|---|---|
| | | | **Y (%)** | **N (%)** | **na (%)** |
| 1(cat.A) | The disease is not present in the territory of the Union OR present only in exceptional cases (irregular introductions) OR present only in a very limited part of the territory of the Union | NC | 20 | 80 | 0 |
| 1(cat.B) | The disease is present in the whole OR part of the Union territory with an endemic character AND (at the same time) several Member States or zones of the Union are free of the disease | NC | 80 | 20 | 0 |

NC: non-consensus; number of judges: 10.

Reasoning supporting the judgement

Supporting Yes for 1 (cat.A):

- These serotypes have been detected only in a very limited part of the Union.

supporting Yes for 1 (cat.B):

- BTV-25–30 is only known to be endemic in a limited part of the Union, e.g. in the South of Sardinia. Insufficient surveillance has been conducted to determine the exact distribution in the Union.

**Table 17:** Outcome of the expert judgement related to criterion 2.1 of Article 9 for all strain groups

| **Question** | | **Final outcome** | **Response** | | |
|---|---|---|---|---|---|
| | | | **Y (%)** | **N (%)** | **na (%)** |
| 2.1 (cat.A) | The disease is highly transmissible | NC | 9 | 91 | 0 |

NC: non-consensus; number of judges: 12.

Reasoning supporting the judgement

Supporting Yes:

- The introduction of the virus into naive populations by spread of infected vectors (e.g. windborne) or movement of viremic hosts, if happening in a suitable season and environment, will lead to explosive transmission. From previous EFSA outputs based on mathematical models, the expected level of vector transmission of BTV is high in the EU, with $R_0$ values between 3 and 10. Several factors are contributing to these high $R_0$ values, such as the long

infectious periods in the host reported in experimental infections (e.g. medians of 17.5, 16.5, 21.3 and 16.5 dpi for EHDV, KASV, BTV and EEV, respectively).

Supporting No:

- Due to high variability in the transmission linked to biotic (host, vectors) and abiotic factors (climatic factors, seasonality), BT cannot be considered generally highly transmissible.

**Table 18:** Outcome of the expert judgement related to criterion D of Article 9 for BTV (1–24) and BTV-16

| Question | | Final outcome | Response | | |
|---|---|---|---|---|---|
| | | | Y (%) | N (%) | na (%) |
| D | The risk posed by the disease in question can be effectively and proportionately mitigated by measures concerning movements of animals and products in order to prevent or limit its occurrence and spread | NC | 50 | 50 | 0 |

NC = non-consensus; number of judges: 10.

Reasoning supporting the judgement

Supporting Yes:

- The risks of health consequences posed, particularly to naïve populations, are substantial. Movement controls can limit risk, but within the context of ongoing transmission from a vector-borne infection. It would still depend on vaccination.
- The occurrence and spread can be limited to some extent in some circumstances, e.g. confined areas (e.g. on the Balearic Islands) or where relevant vectors are not very abundant (e.g. in Norway).

Supporting No:

- Measures in addition to movement restrictions would be needed to control the spread, e.g. vaccination. For example, in France the disease has spread during a few months with movement restrictions in place.

### 3.5.2. Outcome of the assessment of criteria in Annex IV for bluetongue for the purpose of categorisation as in Article 9 of the AHL

As from the legal text of the AHL, a disease is considered fitting in a certain category (A, B, C, D or E corresponding to point (a) to point (e) of Article 9(1) of the AHL) if it is eligible to be listed for Union intervention as laid down in Article 5(3) and fulfils all criteria of the first set from 1 to 2.4 and at least one of the second set of criteria from 3 to 5(d) as shown in Tables 11–15. According to the assessment methodology (EFSA AHAW Panel, 2017b), a criterion is considered fulfilled when the outcome is 'Yes'. With respect to different type of impact where the assessment is divided into current and potential impact, a criterion will be considered fulfilled if at least one of the two outcomes is 'Y' and, in case of no 'Y', the assessment is inconclusive if at least one outcome is 'NC'.

A description of the outcome of the assessment of criteria in Annex IV for bluetongue for the purpose of categorisation as in Article 9 of the AHL is presented in Tables 19, 20 and 21.

**Table 19:** Outcome of the assessment of criteria in Annex IV for BTV -1–24 for the purpose of categorisation as in Article 9 of the AHL (CI = current impact; PI = potential impact)

| Category | Article 9 criteria | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | 1° set of criteria | | | | | 2° set of criteria | | | | | |
| | 1 | 2.1 | 2.2 | 2.3 | 2.4 | 3 | 4 | 5a | 5b | 5c | 5d |
| | Geographical distribution | Transmissibility | Routes of transmission | Multiple species | Morbidity and mortality | Zoonotic potential | Impact on economy | Impact on society | Impact on animal welfare | Impact on environment | Impact on biodiversity |
| A | N | NC | Y | Y | Y | N | Y | CI: N<br>PI: Y | Y | N | N |
| B | Y | Y | Y | Y | Y | N | Y | CI: N<br>PI: Y | Y | N | N |
| C | Y | Y | Y | Y | N | N | N | CI: N<br>PI: Y | Y | N | N |
| D | NC | | | | | | | | | | |
| E | Y | | | | | | | | | | |

**Table 20:** Outcome of the assessment of criteria in Annex IV for BTV-25–30 for the purpose of categorisation as in Article 9 of the AHL

| Category | Article 9 criteria | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | 1° set of criteria | | | | | 2° set of criteria | | | | | |
| | 1 | 2.1 | 2.2 | 2.3 | 2.4 | 3 | 4 | 5a | 5b | 5c | 5d |
| | Geographical distribution | Transmissibility | Routes of transmission | Multiple species | Morbidity and mortality | Zoonotic potential | Impact on economy | Impact on society | Impact on animal welfare | Impact on environment | Impact on biodiversity |
| A | NC | NC | na | Y | N | N | N | N | N | N | N |
| B | NC | Y | na | Y | N | N | N | N | N | N | N |
| C | N | Y | Y | Y | N | N | N | N | N | N | N |
| D | N | | | | | | | | | | |
| E | N | | | | | | | | | | |

**Table 21:** Outcome of the assessment of criteria in Annex IV for BTV-16 for the purpose of categorisation as in Article 9 of the AHL

| Category | Article 9 criteria | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | 1° set of criteria | | | | | 2° set of criteria | | | | | |
| | 1 | 2.1 | 2.2 | 2.3 | 2.4 | 3 | 4 | 5a | 5b | 5c | 5d |
| | Geographical distribution | Transmissibility | Routes of transmission | Multiple species | Morbidity and mortality | Zoonotic potential | Impact on economy | Impact on society | Impact on animal welfare | Impact on environment | Impact on biodiversity |
| A | N | NC | Y | Y | N | N | N | N | N | N | N |
| B | Y | N | Y | Y | N | N | N | N | N | N | N |
| C | Y | N | Y | Y | N | N | N | N | N | N | N |
| D | N | | | | | | | | | | |
| E | N | | | | | | | | | | |

According to the assessment here performed, BT complies with the following criteria of the Sections 1–5 of Annex IV of the AHL for the application of the disease prevention and control rules referred to in points (a) to (e) of Article 9(1):

1) To be assigned to category A, a disease needs to comply with all criteria of the first set (1, 2.1–2.4) and according to the assessment BTV (1–24) complies with criteria 2.2, 2.3 and 2.4, but not with 1 and the assessment is inconclusive on criterion 2.1. BTV-25–30 complies with criterion 2.3, but not with 2.4. The assessment is not applicable on criterion 2.2 and inconclusive on compliance with criteria 1 and 2.1. BTV-16 complies with criteria 2.2 and 2.3, but not with 1 and 2.4 and the assessment is inconclusive on compliance with criterion 2.1. To be eligible for category A, a disease needs to comply additionally with one of the criteria of the second set (3, 4, 5a–d) and BTV (1–24) complies with criteria 4, 5a and 5b, but not with criteria 3, 5c and 5d. BTV-25–30 and BTV-16 do not comply with any of them.
2) To be assigned to category B, a disease needs to comply with all criteria of the first set (1, 2.1–2.4) and according to the assessment BTV (1–24) complies with all of them. BTV-25–30 complies with criteria 2.1 and 2.3, but not with criterion 2.4. The assessment is not applicable on criterion 2.2 and inconclusive on compliance with criterion 1. BTV-16 complies with criteria 1, 2.2 and 2.3, but not with criteria 2.1 and 2.4. To be eligible for category B, a disease needs to comply additionally with one of the criteria of the second set (3, 4, 5a–d) and BTV (1–24) complies with criteria 4, 5a and 5b, but not with criteria 3, 5c and 5d. Therefore, the BTV strain group BTV-1–24 meets the criteria of Section 2 of Annex IV of the AHL. BTV-25–30 and BTV-16 do not comply with any of them.
3) To be assigned to category C, a disease needs to comply with all criteria of the first set (1, 2.1–2.4) and according to the assessment BTV (1–24) complies with criteria 1, 2.1, 2.2 and 2.3, but not with 2.4. BTV-25–30 complies with criteria 2.1, 2.2 and 2.3, but not with 1 and 2.4. BTV-16 complies with criteria 1, 2.2 and 2.3, but not with 2.1 and 2.4. To be eligible for category C, a disease needs to comply additionally with one of the criteria of the second set (3, 4, 5a–d) and BTV (1–24) complies with criteria 5a and 5b, but not with criteria 3, 4, 5c and 5d. BTV-25–30 and BTV-16 do not comply with any of them.
4) To be assigned to category D, a disease needs to comply with criteria of Sections 1, 2, 3 or 5 of Annex IV of the AHL and with the specific criterion D of Section 4, for which the outcome for BTV (1–24) is inconclusive. BTV-25–30 and BTV-16 do not fulfil criteria of Sections 1, 2, 3 or 5 of Annex IV of the AHL.

5) To be assigned to category E, a disease needs to comply with criteria of Sections 1, 2 or 3 of Annex IV of the AHL and/or the surveillance of the disease is necessary for reasons relating to animal health, animal welfare, human health, the economy, society or the environment. The latter is applicable if a disease fulfils the criteria as in Article 5, with which BTV (1–24) complies, but not BTV-25–30 or BTV-16.

## 3.6. Assessment of Article 8

This section presents the results of the assessment on the criteria of Article 8(3) of the AHL about bluetongue. The Article 8(3) criteria are about animal species to be listed, as it reads below:

'3. Animal species or groups of animal species shall be added to this list if they are affected or if they pose a risk for the spread of a specific listed disease because:

a) they are susceptible for a specific listed disease or scientific evidence indicates that such susceptibility is likely; or
b) they are vector species or reservoirs for that disease, or scientific evidence indicates that such role is likely.'

For this reason the assessment on Article 8 criteria is based on the evidence as extrapolated from the relevant criteria of Article 7, i.e. the ones related to susceptible and reservoir species or routes of transmission, which cover also possible role of biological or mechanical vectors.[9] According to the mapping, as presented in Table 5, Section 3.2 of the scientific opinion on the ad hoc methodology (EFSA AHAW Panel, 2017b), the main animal species to be listed for bluetongue serotypes/strain groups according to the criteria of Article 8(3) of the AHL are as displayed in Table 22.

**Table 22:** Main animal species to be listed for BT serotypes/strains according to criteria of Article 8 (for details see Section 3.3.1.1)

| | | Order | Family | Genus/species |
|---|---|---|---|---|
| Susceptible* | BTV-1–24 (including BTV-16) | Artiodactyla | Bovidae | Several species, potentially all |
| | | | Cervidae | Several species, potentially all |
| | | | Camelidae | Several species, potentially all |
| | BTV-25–30 | Artiodactyla | Bovidae | *Ovis aries, Capra hircus* |
| Reservoir | BTV-1–24 (including BTV-16) | Artiodactyla | Bovidae | *Bos taurus*, *Ovis aries* |
| | | | Cervidae | *Cervus elaphus* |
| | BTV-25, -27, 30 | Artiodactyla | Bovidae | *Ovis aries*, *Capra hircus* |
| Vectors | BTV-1–24 (including BTV-16) | Diptera | Ceratopogonidae | *Culicoides* spp. |
| | BTV-25, -27, -30 | None | | |

*: Zoo animals are not included in this table, since they are not present in large number in the EU. Some carnivores have been demonstrated to be susceptible, although they may not be epidemiologically important.

# 4. Conclusions and recommendations

## 4.1. Conclusions

***ToR 4.2*** *Assess, by using appropriate criteria, the feasibility of grouping the currently known BTV serotypes in appropriately defined groups of serotypes sharing similar properties thus creating a number of 'BTV serotype groups' separated by significant different levels of impact on animal health (e.g. most serious clinical symptoms in many individuals in large areas, mild symptoms to few individuals within small areas or no symptoms at all in one or more BT susceptible species etc.).*

- Repeated incursions of BT into Europe have been caused by different BTV strains, including multiple serotypes, almost every year since 1998.

[9] A vector is a living organism that transmits an infectious agent from an infected animal to a human or another animal. Vectors are frequently arthropods. Biological vectors may carry pathogens that can multiply within their bodies and be delivered to new hosts, usually by biting. In mechanical vectors the pathogens do not multiply within the vector, which usually remains infected for shorter time than in biological vectors.

- The serotype classification is useful for the production of serotype-specific vaccines, able to protect against the homologous BTV, but the classification based on serotypes is not sufficient to fully represent the genomic diversity and pathogenic heterogeneity of BTV: different virus strains belonging to the same serotypes have had very different impacts on animal health in outbreaks in Europe and elsewhere. Similar patterns could also be expected in the future, with novel BTV strains occurring in Europe.
- For this reason, the assessment has been based on BTV strains rather than serotypes, thus merging the classification according to serotype and genetic diversity (genotype) with other aspects of epidemiological relevance and animal health impact, including the time period and geographical area of occurrence.
- A number of criteria were considered when analysing the animal health impacts of different BTV strains including the intraherd morbidity, mortality and case-fatality rates for each BTV strain, the mean number of outbreaks per week, and the ability to actively circulate within different episystems, as calculated from ADNS data;
- The prediction of the impact of BTV strains is strongly hampered by knowledge gaps, and therefore the field observations are of paramount importance, both in the EU and in neighbouring countries.

***ToR 4.3*** *Review and classify the existing serotypes according to the outcome of the assessment in point 4.2 above and assess whether any of the above serotypes/groups of serotype could be candidates for a partial or total exclusion from the overall BT policy currently in place in the EU, in particular due to their low level of virulence or pathogenicity.*

- According to the assessment, the only BTV serotypes that could be partially excluded from the overall BT policy currently in place in the EU, due to their low level of virulence or pathogenicity, are the small ruminant-adapted strains, i.e. BTV strains belonging to serotypes BTV-25, -26, -27 and related isolates.

***ToR 5.1*** *Considering the outcome of the assessments and reviews referred to in paragraph 4 above, for each of the aforementioned groups of serotypes, or BT in general as appropriate, assess, following the criteria laid down in Article 7 of the AHL, its eligibility of being listed for Union intervention as laid down in Article 5(3) of the AHL;*

- According to the assessment here performed, BTV (1–24) complies with all criteria of the first set and with three criteria of the second set and therefore can be considered eligible to be listed for Union intervention as laid down in Article 5(3) of the AHL. BTV-25–30 and BTV-16 do not comply with criterion 5 A(iii) of the first set and therefore cannot be considered eligible to be listed for Union intervention as laid down in Article 5(3) of the AHL.

***ToR 5.2a*** *For each of the aforementioned groups of serotypes, or for BT in general, if found eligible to be listed for Union intervention, provide an assessment of its compliance with each of the criteria in Annex IV to the AHL for the purpose of categorisation of diseases in accordance with Article 9 of the AHL;*

- According to the assessment here performed, BTV (1–24) meets the criteria as in Sections 2 and 5 of Annex IV of the AHL, for the application of the disease prevention and control rules referred to in points (b) and (e) of Article 9(1) of the AHL. Since BTV-25–30 and BTV-16 cannot be considered eligible to be listed for Union intervention as laid down in Article 5(3) of the AHL, the assessment of its compliance with each of the criteria in Annex IV to the AHL for the purpose of categorisation of diseases in accordance with Article 9 of the AHL is not applicable.

***ToR 5.2b*** *For each of the aforementioned groups of serotypes, or for BT in general, if found eligible to be listed for Union intervention, provide a list of animal species that should be considered candidates for listing in accordance with Article 8 of the AHL.*

- According to the assessment performed here, the animal species that can be considered for listing for BTV-1–24 according to Article 8(3) of the AHL are as reported in Table 22 in Section 3.6 of the present document: several (potentially all) species of Arctiodactyla belonging to the families of Bovidae, Cervidae and Camelidae as susceptible species; domestic cattle, sheep and red deer as reservoir hosts; midges insect of genus *Culicoides* spp. as vector species for BTV-1–24.

- Since BTV-25–30 and BTV-16 cannot be considered eligible for listing for Union intervention as laid down in Article 5(3) of the AHL, the assessment of the animal species that are considered to be listed in accordance with Article 8 of the AHL is not applicable.

## 4.2. Recommendations

Regarding ToR 4.3 about the BTV serotypes and strains that could be candidates for exclusion from the overall BT policy currently in place in the EU, and ToR 5 about criteria of Article 5 and 9 of AHL for assessing whether and which specific rules for the prevention and control would apply to BT, some recommendations are here presented about the importance of surveillance and control of BTV and related knowledge gaps**:**

- Surveillance data and knowledge of BTV strains and serotypes circulating in 'source regions' outside Europe is needed to provide a better understanding/prediction of the likelihood of an incursion into/outbreak in Europe, via known geographic pathways, and the risk to European animal populations should such an incursion occur.
- Surveillance is also needed to detect new BT outbreaks within Europe, to identify both their significance (severity, rate of spread, serotype, genotype and host species involvement) and to inform the development of appropriate control strategies. For this reason, surveillance is needed both within the EU and in neighbouring areas that can be a source of future incursions.
- Appropriate surveillance strategies/methods, including sentinels and the importance of passive surveillance, should be refined and publicised.
- It would be helpful to have a well-established and identified surveillance network to detect outbreaks at an early stage, in order to characterise the virus in cause and to assess their relative economic importance and their impact on animal health.
- If new outbreaks can be identified early on, then an appropriate 'ring vaccination' strategy could be developed to reduce/prevent viral spread and the potential for further outbreaks.
- If a broader cross-reactive (cross-serotype) BTV vaccine (ideally with DIVA capability and long shelf-life) could be developed, this would potentially reduce the number of different vaccine preparations required and therefore potentially reduce the costs of a vaccine bank.

**Research needs**

- There are important knowledge gaps with potential implications on future threats caused by BTV incursions/persistence in Europe. Therefore, more knowledge would be helpful concerning:
  - Genetic markers in the virus for severe clinical signs/pathogenesis.
  - Genetic markers in the virus for efficient vector transmission by different vector populations within the different episystems indentified in Europe. To do this, better resources, including new vector-colonies and cell-lines for European vector species would be particularly helpful.
  - The risks posed by potential reassortment of genetic information among existing and novel serotypes in the field. It is not known whether this could lead to novel virus strains with new biological characteristics, or new combinations of existing characteristics.
  - The role of other vector species in the transmission of the novel serotypes.
  - The persistence of virus including novel types in semen and abilities for vertical transmission need more information.

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## Abbreviations

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| ADNS | Animal Disease Notification System |
| AGID | agar gel immunodiffusion |
| AHAW | EFSA Panel on Animal Health and Welfare |
| AHL | Animal Health Law |
| BT | bluetongue |
| BTV | bluetongue virus |
| BWC | beef weaned calves |
| CDC | Centers for Disease Control and Prevention |
| CFSPH | Center for Food Security and Public Health |
| CFT | complement fixation test |
| CI | confidence interval |
| CITES | Convention on International Trade in Endangered Species of Wild Fauna and Flora |
| CVMP | Committee for Medicinal Products for Veterinary Use |
| DEET | diethyl toluamide |
| DIVA | distinguish infected from vaccinated animals |
| EEV | equine encephalosis virus |
| EHDV | epizootic hemorrhagic disease virus |
| ELISA | enzyme-linked immunosorbent assay |
| FDA | Food and Drug Administration |
| FMD | foot and mouth disease |
| GMP | Good Manufacturing Practice |
| ICBA | Individual and Collective Behavioural Aggregation |

| | |
|---|---|
| IgG | immunoglobulin G |
| IUCN | International Union for Conservation of Nature |
| KASV | Palyam virus |
| LAV | live attenuated vaccine |
| MRP | Movement restriction policy |
| MS | Member State |
| NSAID | non-steroidal anti-inflammatory drugs |
| OIE | World Organization for Animal Health |
| PCR | polymerase chain reaction |
| RNA | ribonucleic acid |
| RT-PCR | reverse transcription polymerase chain reaction |
| RTS | return to service |
| SN | seroneutralisation/serum neutralisation |
| ToR | Terms of Reference |
| TPT | transplacental transmission |
| VP | viral protein |